TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

TWENTY-EIGHTH SESSION

HELD AT THE NEW WILLARD HOTEL, WASHINGTON
MAY 8, 9 AND 10, 1916

EDITED BY
LINNAEUS EDFORD LA FÉTRA, M.D.

VOLUME XXVIII

CONTENTS

PRESIDENTS

1889. A. Jacobi, M.D.
1890. J. Lewis Smith, M.D.
1891. T. M. Rotch, M.D.
1892. Wm. Osler, M.D.
1893. A. D. Blackader, M.D.
1894. John M. Keating, M.D.
1895. F. Forchheimer, M.D.
1896. Joseph O'Dwyer, M.D.
1897. Samuel S. Adams, M.D.
1898. L. Emmett Holt, M.D.
1899. Wm. P. Northrup, M.D.
1900. Henry Koplik, M.D.
1901. Wm. D. Booker, M.D.
1902. W. S. Christopher, M.D.
1903. J. P. Crozer Griffith, M.D.
1904. Augustus Caillé, M.D.
1905. C. G. Jennings, M.D.
1906. A. Jacobi, M.D.
1907. B. K. Rachford, M.D.
1908. C. G. Kerley, M.D.
1909. Charles P. Putnam, M.D.
1910. David L. Edsall, M.D.
1911. Henry Dwight Chapin, M.D.
1912. Walter Lester Carr, M.D.
1913. John Lovett Morse, M.D.
1914. Samuel McC. Hamill, M.D.
1915. George N. Acker, M.D.
1916. Rowland G. Freeman, M.D.

OFFICERS, 1916

President ..... Rowland G. Freeman, M.D.
Vice President ..... J. C. Gittings, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.
Assistant Editor ..... O. M. Schloss, M.D.

COUNCIL

L. E. La Fétra, M.D., *Chairman*

Isaac A. Abt, M.D.
John Howland, M.D.
Fritz B. Talbot, M.D.
D. M. Cowie, M.D.
L. Emmett Holt, M.D.
Charles A. Fife, M.D.

MEETING PLACES

1888. Washington, D. C. (Organization), September 18.
1889. Washington and Baltimore, September 20 and 21.
1890. New York, June 3 and 4.
1891. Washington, September 22 and 25.
1892. Boston, May 2, 3 and 4.
1893. West Point, N. Y., May 24, 25 and 26.
1894. Washington, May 29 and June 1.
1895. Virginia Hot Springs, May 27, 28 and 29.
1896. Montreal, May 25, 26 and 27.
1897. Washington, May 4, 5 and 6.
1898. Cincinnati, June 1, 2 and 3.
1899. Deer Park, June 27, 28 and 29.
1900. Washington, May 1, 2 and 3.
1901. Niagara Falls, May 27, 28 and 29.
1902. Boston, May 26, 27 and 28.
1903. Washington, May 12, 13 and 14.
1904. Detroit, May 30, 31 and June 1.
1905. Lake George, N. Y., June 19, 20 and 21.
1906. Atlantic City, N. J., May 30, 31 and June 1.
1907. Washington, May 7, 8 and 9
1908. Delaware Water Gap, May 25, 26 and 27.

1909. Lenox, Mass., May 27 and 28.
1910. Washington, May 3, 4 and 5.
1911. Lake Mohonk, N. Y., May 31 and June 1 and 2.
1912. Hot Springs, Va., May 29, 30 and 31.
1913. Washington, May 5, 6 and 7.
1914. Stockbridge, Mass., May 26, 27 and 28.
1915. Lakewood, N. J., May 24, 25 and 26.
1916. Washington, May 8, 9 and 10.
1917. White Sulphur Springs, W. Va., May 28, 29 and 30.

OFFICERS 1917

President ..... Frank S. Churchill, M.D.
Vice President ..... Wilder Tileston, M.D.
Secretary ..... Howard C. Carpenter, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
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D. M. Cowie, M.D. — Royal S. Haynes, M.D.

MEMBERS

1903. Abt, Isaac A., M.D. ..... 4810 Kenwood Avenue, Chicago
1893. Acker, George N., M.D. ..... 913 Sixteenth Street, Washington
O Adams, Samuel S., M.D. ..... 1801 Connecticut Ave., N. W., Washington
1916. Bartlett, Frederic H., M.D. ..... 44 East 63d Street, New York
O Blackader, A. D., M.D. ..... 236 Mountain Street, Montreal
1916. Blackfan, Kenneth D., M.D. ..... Johns Hopkins Hospital, Baltimore
1911. Bowditch, Henry I., M.D. ..... 416 Marlborough Street, Boston
1911. Butterworth, William W., M.D. 3914 Prytania Street, New Orleans, La.
O Caillé, Augustus, M.D. ..... 753 Madison Avenue, New York
1911. Carpenter, Howard C., M.D. ..... 1805 Spruce Street, Philadelphia
O Carr, Walter Lester, M.D. ..... 68 West Fifty-First Street, New York
O Chapin, Henry Dwight, M.D. ..... 51 West Fifty-First Street, New York
1897. Churchill, F. S., M.D. ..... 1259 North State Street, Chicago
1910. Coit, Henry L., M.D. ..... 277 Mt. Prospect Avenue, Newark, N. J.
1909. Cowie, D. M., M.D. ..... Lawrence Building, Ann Arbor, Mich.
1891. Crandall, Floyd M., M.D. ..... 113 West Ninety-Fifth Street, New York
O Dorning, John, M.D. ..... 124 West Eighty-First Street, New York
1906. Dunn, Charles Hunter, M.D. ..... 178 Marlborough Street, Boston
1904. Eaton, Percival J., M.D. ..... 715 N. Highland Avenue, E. E., Pittsburgh
1907. Fife, Charles A., M.D. ..... 2033 Locust Street, Philadelphia
1895. Freeman, Rowland G., M.D. 211 West Fifty-Seventh Street, New York
1913. Friedlander, Alfred, M.D. ..... 4 West Seventh Street, Cincinnati
1913. Gerstenberger, Henry J., M.D. ..... Osborn Building, Cleveland
1910. Gittings, J. C., M.D. ..... 3492 Chestnut Street, Philadelphia
1897. Graham, E. E., M.D. ..... 1713 Spruce Street, Philadelphia
1892. Griffith, J. P. Crozer, M.D. ..... 1810 Spruce Street, Philadelphia
1898. Hamill, S. McC., M.D. ..... 1822 Spruce Street, Philadelphia
1902. Hand, Alfred, Jr., M.D. ..... 1724 Pine Street, Philadelphia
1910. Haynes, Royal S., M.D. ..... 213 West Seventieth Street, New York
1909. Heiman, Henry, M.D. ..... 64 West Eighty-Fifth Street, New York

1914. Helmholz, Henry F., M.D.....1005 Michigan Avenue, Evanston, Ill.
1910. Herrman, Charles, M.D.....250 West Eighty-Sixth Street, New York
1915. Hess, Alfred F., M.D.....16 West Eighty-Sixth Street, New York
O Holt, L. Emmett, M.D.....14 West Fifty-Fifth Street, New York
1913. Hoobler, B. Raymond, M.D.....1563 David Whitney Building, Detroit
1905. Howland, John, M.D.....20 East Eager Street, Baltimore
O Jacobi, A., M.D.....19 East Forty-Seventh Street, New York
1896. Kerley, Charles G., M.D.....132 W. Eighty-First Street, New York
1905. Knox, J. H. Mason, M.D.....“The Severn,” Baltimore
O Koplik, Henry, M.D.....30 East Sixty-Second Street, New York
1903. Ladd, Maynard, M.D.....270 Clarendon Street, Boston
1903. La Fétra, Linnæus E., M.D.....113 East Sixty-First Street, New York
1911. Lucas, William Palmer, M.D..University of California, San Francisco
1912. McClanahan, H. M., M.D.....468 Brandeis Building, Omaha
1909. Machell, H. T., M.D.....216 St. Clair Avenue, Toronto
1898. Miller, D. J. Milton, M.D.....127 S. Illinois Avenue, Atlantic City, N. J.
1896. Morse, J. Lovett, M.D.....70 Bay State Road, Boston
1908. Nicoll, Matthias, Jr., M.D.....124 East Sixtieth Street, New York
O Northrup, William P., M.D..57 East Seventy-Ninth Street, New York
1915. Park, Edwards A., M.D.....Johns Hopkins Hospital, Baltimore
1910. Pisek, Godfrey R., M.D.....26 East Sixty-Fourth Street, New York
1912. Porter, R. Langley, M.D.....240 Stockton Street, San Francisco
1891. Rachford, B. K., M.D.....1961 Madison Road, Cincinnati
1905. Ruhräh, John, M.D.....11 Chase Street, Baltimore
1900. Saunders, E. W., M.D.....3003 Lafayette Avenue, St. Louis
1912. Schloss, Oscar M., M.D.....172 West Seventy-Ninth Street, New York
1913. Sedgwick, Julius P., M.D.....2015 Kenwood Parkway, Minneapolis
1902. Shaw, Henry L. K., M.D.....361 State Street, Albany
1914. Sherman, DeWitt H., M.D.....680 West Ferry Street, Buffalo
1915. Smith, Richard M., M.D.....329 Beacon Street, Boston
1891. Snow, Irving M., M.D.....737 Delaware Avenue, Buffalo
1905. Southworth, Thomas S., M.D.....807 Madison Avenue, New York
1911. Talbot, Fritz B., M.D.....311 Beacon Street, Boston
1910. Tileston, Wilder, M.D.....424 Temple Street, New Haven
1914. Van Ingen, Philip, M.D.....125 East Seventy-First Street, New York
1912. Veeder, Borden S., M.D.....500 S. Kingshighway, St. Louis
1914. Walls, Frank X., M.D.....1208-30 North Michigan Boulevard, Chicago
1896. Westcott, Thompson S., M.D.....1720 Pine Street, Philadelphia
1913. Wilcox, Herbert B., M.D.....159 East Seventieth Street, New York
O Winters, J. E., M.D.....25 West Thirty-Seventh Street, New York

Note.—The first column gives the date of election to the Society. The organizers of the Society are designated by “O,” the date being 1888.

HONORARY MEMBERS

Dr. John Thompson.....Edinburgh, Scotland
Dr. George F. Still.....London, England
Dr. O. Heubner.....Berlin, Germany
Dr. William Osler.....Oxford, England
Dr. A. Baginsky.....Berlin, Germany
Dr. V. Hutinel.....Paris, France
Dr. Charles Rauchfuss.....Petrograd, Russia

EMERITUS MEMBERS

Dr. Allen Baines.....Toronto
Dr. Francis Huber.....New York
Dr. John Dorning.....New York

Deceased

John A. Jeffries, M.D.
Born, September 2, 1859,
Died, March 26, 1892.

Thomas F. Sherman, M.D.
Born, March 17, 1856,
Died, September 26, 1893.

John M. Keating, M.D.
Born, April 20, 1852,
Died, November 17, 1893.

Charles Warrington Earle, M.D.
Born, 1845,
Died, November 19, 1893.

J. Lewis Smith, M.D.
Born, October 15, 1827,
Died, June 9, 1897.

Joseph O'Dwyer, M.D.
Born, October 12, 1841,
Died, January 7, 1898.

John Henry Fruitnight, M.D.
Born, November 9, 1851,
Died, December 18, 1900.

Frederick A. Packard, M.D.
Born, November 17, 1862,
Died, November 1, 1902.

Walter S. Christopher, M.D.
Born, 1859,
Died, March 2, 1905.

Leroy Milton Yale, M.D.
Born, February 12, 1841,
Died, September 12, 1906.

James Park West, M.D.
Born, June 27, 1858
Died, June 25, 1908.

Frederick Forchheimer, M.D.
Born, 1853,
Died, June 1, 1913.

Thomas Morgan Rotch, M.D.
Born, 1850,
Died, March 9, 1914.

Charles P. Putnam, M.D.
Born, 1845,
Died, April 22, 1914

CONSTITUTION AND BY-LAWS OF THE AMERICAN PEDIATRIC SOCIETY

ARTICLE I

Name and Object of the Society

The Society shall be known as the American Pediatric Society, and shall hold an annual meeting.

It has for its object the advancement of the knowledge of physiology, pathology and therapeutics of infancy and childhood.

ARTICLE II

Proceedings

The proceedings shall consist of:

1. Discussions on subjects previously selected.
2. Original communications.
3. Demonstrations of gross and microscopic preparations, apparatus, and instruments.

ARTICLE III

Members

The Society shall be composed of three classes of members to be designated: (1) active members; (2) emeritus members, and (3) honorary members.

The number of active members shall be limited to seventy-five.

The number of emeritus members shall be unlimited.

The number of honorary members shall be limited to twenty-five.

ARTICLE IV

Election of Active Members

Nominations to membership, signed by two members of the Society, must be made in writing at least one meeting prior to election.

Nominations should be made to the Secretary, whose duty it shall be to require the nominators to write a personal letter endorsing and stating the qualifications of the nominee, and at the same time furnishing a list of the nominee's professional position and publications, with reprints of the latter, when obtainable.

It shall be the duty of the Secretary to transmit to the Chairman of the Council all the above papers pertaining to each nominee, at least three months prior to his possible election. *

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* In the event that required information relating to candidates for membership is not furnished to the Secretary by three months before the time of the meeting at which they would be considered, such candidates for election shall be held over for another year. (Resolution adopted 1912.)

The Chairman of the Council shall transmit the above-named papers to the other members of the Council in the order of their seniority as Council members, the junior member of the Council returning them to the Secretary.

It shall also be the duty of the Secretary to furnish a printed list of all nominees at least once a year to every member of the Society, and it shall be the duty of the members of the Society, without solicitation, to furnish the Council with any information that they may possess as to the fitness of the nominees to become members of the Society.

On nomination by the Council, members shall be elected by the Society by ballot. A two-thirds vote of the members present shall be necessary for election.

ARTICLE V

Election of Emeritus and Honorary Members

Active members who have served fifteen years and have paid all their dues, may on their request and on the recommendation of the Council be made emeritus members. They shall be entitled to attend meetings and read papers, when they so desire, but cannot vote.

Physicians of sufficient eminence to merit the distinction may be elected honorary members, to a number not exceeding twenty-five. Such members shall be entitled to attend all meetings and take part in the proceedings, but cannot vote. Honorary members shall be elected in the same way as active members.

ARTICLE VI

Initiation Fee and Annual Dues

Election to membership shall be completed by the payment of an initiation fee of $10.

Each active member shall pay an annual fee, the amount of which shall be decided at each annual meeting.

Emeritus and honorary members shall be exempt from fees.

ARTICLE VII

Officers

The officers shall consist of a President, Vice-President, Secretary, Recorder [and Editor], Treasurer and a Delegate to the Congress of Physicians and Surgeons.

The officers shall be elected annually on nomination by the Council.

ARTICLE VIII

Duties of Officers

The duties of the President, Vice-President, Secretary and Treasurer shall be those usual to these offices. The Recorder [and Editor] shall secure the papers read and see that proper notes are taken of the discussion thereon for the use of the committee on publication.

ARTICLE IX

The Council

The Council shall consist of seven members, the senior member being Chairman. One member of the Council shall be elected each year. Four member shall constitute a quorum. The senior member shall retire at the end of each year and shall not be immediately eligible to reelection.

ARTICLE X

Duties of Council

The duties of the Council shall be to consider nominations for membership and report them to the Society. The votes of four members of the Council shall be required for nomination. The Council shall also nominate the officers of the Society and shall decide the time and place of meeting.

ARTICLE XI

Committee of Arrangements

The President, Secretary and the Chairman of the Council shall constitute a committee of arrangements, the President being chairman of this committee. They shall arrange the details of the meeting and the preparation of the program, and they shall have the authority to invite guests to attend the meeting and to participate in the discussion

ARTICLE XII

Publication Committee

The Secretary, Treasurer and Recorder shall constitute a committee on publication, to which shall be referred all papers, reports and other matters intended for publication.

All papers presented shall become the property of the Society.

ARTICLE XIII

Amendment of Constitution and By-Laws

Proposals for amendments of the constitution and by-laws must have been made at the meeting previous to that at which they are

voted on, the notice for which shall contain an announcement of the proposed changes. Such changes shall require, for their adoption, an affirmative vote of three-fourths of the active members present.

ARTICLE XIV

Termination of Membership

A member may be expelled from the Society for conduct unbecoming a physician and a gentleman. In such cases, formal charges must be made in writing by two members, which shall be referred to the Council.

Active membership shall lapse for any one of the following reasons:

(1) Absence from three consecutive meetings without excuse acceptable to the council; (2) failure to present and read a paper for five consecutive years; the Secretary in both these cases shall notify members one year before date of possible lapse; (3) non-payment of dues for two years, two notifications having been sent by the Treasurer.

ARTICLE XV

Quorum

Any number of members present at the appointed time of the annual meeting, shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for the expulsion of members, or for altering the constitution and by-laws, twenty-five members shall be necessary.

ARTICLE XVI

Order of Business

1. The President shall call the meeting to order and deliver an annual address. In his absence the Vice-President shall preside, and in the absence of all these officers, the Chairman of the Council.

2. When a general discussion is arranged by the Council, the two members appointed to open the discussion shall not occupy more than twenty minutes each; subsequent speakers shall be restricted to ten minutes each.

3. Papers shall not exceed fifteen minutes in the reading. In the discussion following the reading of such papers, remarks shall be limited to five minutes. Should any paper be too long to read in

fifteen minutes, the writer must prepare an abstract which can be read within that time.*

4. At the business session the report of the Council as a committee on nominations to office and to membership, shall be made, and ballot shall be held thereon.

Adopted May 28, 1900.

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* In order to expedite the publication of the Transactions all members whose papers are to appear in the volume, be required either to have their articles in the hands of the editor before July 1 or to have them in process of publication in some medical journal by that date. In the latter event, the editor of the Transactions is to be notified what journal will publish the paper and reprints or galley proofs are to be furnished to him as soon as possible. (Resolution adopted 1912.)

MINUTES OF THE TWENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN PEDIATRIC SOCIETY

Held at the New Willard Hotel, Washington, D. C., May 8, 9 and 10, 1916

The meeting was called to order at 10.15 a. m. by the President, Dr. Rowland Godfrey Freeman of New York City.

The following members were present during the sessions: Drs. Isaac A. Abt, Chicago; George N. Acker, Washington; Samuel S. Adams, Washington; A. D. Blackader, Montreal; Henry Ingersol Bowditch, Boston; William W. Butterworth, New Orleans; Howard Childs Carpenter, Philadelphia; Walter Lester Carr, New York; Henry L. Coit, Newark; David M. Cowie, Ann Arbor; Percival J. Eaton, Pittsburgh; Charles A. Fife, Philadelphia; Rowland G. Freeman, New York; Alfred M. Friedlander, Cincinnati; John Claxton Gittings, Philadelphia; Edwin E. Graham, Philadelphia; J. P. Crozer Griffith, Philadelphia; Samuel McC. Hamill, Philadelphia; Henry Heiman, New York; Henry F. Helmholz, Evanston, Ill.; Charles Herrman, New York; Alfred F. Hess, New York; L. Emmett Holt, New York; B. Raymond Hoobler, Detroit; John Howland, Baltimore; Abraham Jacobi, New York; J. H. Mason Knox, Baltimore; Henry Koplik, New York; Maynard Ladd, Boston; Linnæus E. La Fétra, New York; H. M. McClanahan, Omaha; Henry T. Machell, Toronto; D. J. Milton Miller, Atlantic City; John Lovett Morse, Boston; Matthias Nicoll, Jr., New York; Edwards A. Park, Baltimore; B. K. Rachford, Cincinnati; Oscar M. Schloss, New York; Julius P. Sedgwick, Minneapolis; Henry L. K. Shaw, Albany; DeWitt H. Sherman, Buffalo; Richard M. Smith, Boston; Irving M. Snow, Buffalo; Thomas S. Southworth, New York; Fritz B. Talbot, Boston; Wilder Tileston, New Haven; Philip Van Ingen, New York; B. S. Veeder, St. Louis; and Thompson S. Westcott, Philadelphia.

In addition to the members, the following guests were introduced: A. H. Beifeld, Iowa City, Iowa; Alan Brown, Toronto, Ohio; George L. Chapman, Toledo; E. P. Copeland, Washington, D. C.; L. W. Elias, Asheville, N. C.; E. C. Fleischner, San Francisco; W. D. Ford, Detroit; A. D. Holmes, Detroit; Peter C. Kiang, China; C. H. Laws,

Ann Arbor; Prof. Frederic S. Lee, New York City; Frank Leech, Washington, D. C.; McKim Marriott, Baltimore; Hugh McCullough, St. Louis; H. J. Morgan, Toledo; W. A. Mulheim, Augusta, Ga.; Eugene W. Murray, Newark, N. J.; Walter R. Ramsey, St. Paul; Worth Ross, Detroit; J. S. Wall, Washington, D. C.

The Minutes of the Twenty-Seventh Annual Meeting, as published in the Transactions were approved.

The following papers were presented:

1. Dr. Rowland G. Freeman, Presidential Address, on the subject, "Fresh Air."

2. Prof. Frederic S. Lee of Columbia University (by invitation): "Recent Progress on the Physiologic Action of Atmospheric Conditions."

3. Dr. Richard M. Smith: "Some Studies on the Mode of Infection in Pyelitis of Infancy."

The paper was discussed by Drs. Rachford, Helmholz and Smith.

4. Dr. Alfred F. Hess: "Diet and Growth in Infantile Scurvy" (lantern slides).

The paper was discussed by Drs. Holt, Herrman, Adams, Blackader, Shaw, Eaton, Hamill, Coit, Heiman, Van Ingen, Ladd, Freeman and Hess.

5. Drs. George N. Acker and Edgar P. Copeland: "Transient Abdominal Tumor in a Child of Five Years with Redundant Colon" (lantern slides).

6. Dr. Alfred Friedlander: "Sarcoma of the Kidney Treated by the Roentgen Ray."

7. Dr. Henry T. Machell: "Report of a Case of Influenza with Two Unusual Complications."

8. Drs. H. M. McClanahan and A. A. Johnson: "A Brief Report of Sixty Blood Examinations in Infancy, with a Review of the Recent Literature of the Blood in Infants."

The paper was discussed by Drs. Schloss, Sedgwick and Cowie.

9. Drs. Borden S. Veeder and Meredith Johnson: "The Creatin and Creatinin Content of the Blood in Children."

10. Dr. L. E. La Fétra; "The Hospital Care of Premature Infants."

The paper was discussed by Drs. Veeder, Sedgwick, La Fétra and Hoobler.

11. Dr. Maynard Ladd: "Further Experience with Homogenized Olive Oil Mixtures."

The paper was discussed by Drs. Bowditch and Ladd.

12. Drs. Henry I. Bowditch and Alfred W. Bosworth: "A Method for Preparing Synthetic Milk for Studies of Infant Metabolism."

13. Drs. J. C. Gittings, George Fetterolf and A. Graeme Mitchell: "A Study of the Topography of the Pulmonary Lobes and Fissures, with Special Reference to Thoracentesis."

14. Dr. Edwards A. Park: "Deformities of the Costochondral Junctions in Rickets" (lantern slides).

15. Drs. J. C. Gittings, S. McC. Hamill, C. A. Fife, and H. C. Carpenter: "Report of the Committee on Vaginitis."

16. Dr. B. K. Rachford: "Epidemic Vaginitis in Children."

The report of the Committee and the paper of Dr. Rachford were discussed by Drs. Holt, Rachford, Hamill, Adams, Carpenter, Fife, Smith, Carr, Cowie and Freeman.

17. Dr. Alfred F. Hess: "Provocative and Prophylactic Vaccination in the Vaginitis of Infants."

The paper was discussed by Drs. Talbot, Sedgwick and Hess.

18. Dr. B. R. Hoobler: "Some Early Symptoms Suggestive of Protein Sensitization in Infancy."

The paper was discussed by Drs. Schloss, Talbot and Hoobler.

19. Drs. D. M. Cowie and C. H. Laws: "The Calcium Metabolism in a Case of Hemophilia."

The paper was discussed by Drs. Hess, Talbot and Cowie.

20. Drs. John Howland and W. McKim Marriott: "The Calcium Content of the Blood in Rachitis and Tetany."

The paper was discussed by Drs. Cowie, Veeder, Sedgwick, Holt and Marriott.

21. Dr. Thomas S. Southworth: "Early Morning Toxic Vomiting in Children."

The paper was discussed by Drs. Sherman, Talbot, Abt and Southworth.

22. Dr. John Lovett Morse: "A Study of the Etiology of Chorea."

The paper was discussed by Drs. Koplik, Abt, Helmholz, La Fétra, Veeder, Jacobi and Morse.

23. Dr. Henry Heiman: "The Effect of Subcutaneous Injections of Magnesium Sulphate in Chorea."

24. Dr. Edwin E. Graham: "The Prognosis and Treatment of Banti's Disease in Children."

The paper was discussed by Drs. Koplik and Graham.

25. Dr. Isaac A. Abt: "Familial Icterus."

The paper was discussed by Drs. Tileston, Sherman and Abt.

26. Dr. David M. Cowie: "Observations on the Intradermal Injection of Diphtheria Toxin, with Reference to the Schick Test."

The paper was discussed by Drs. Koplik and Hess.

27. Drs. P. J. Eaton and E. B. Woods: "(a) Pertussis-Measles-Pneumonia. (b) Pertussis. (c) Measles-Pertussis-Temporary Chest Deformity. (A group of cases occurring simultaneously in one family.)"

28. Dr. D. J. Milton Miller: "Scarlet Fever and Measles Occurring Simultaneously in the Same Individual, the Other Children of the Family Acquiring Measles Only."

The paper was discussed by Drs. Nicoll and Miller.

29. Dr. Charles Herrman: "Some Observations on Measles."

The paper was discussed by Drs. La Fétra, Koplik, Hamill, Holt and Herrman.

30. Dr. Henry F. Helmholz: "The Bacteriology of the Urine in Healthy Children."

31. Dr. W. W. Butterworth: "Oxycephaly: Its Occurrence in Two Brothers. Review of Literature."

32. Dr. Henry Koplik: "Meningitis in the New-Born and in Infants Below Three Months of Age."

The paper was discussed by Drs. Talbot, Miller, Herrman, Knox, Abt and Koplik.

33. Dr. Edwin E. Graham: "The Use of Salt Solution by the Bowel (Murphy Method) in Infants and Children."

The paper was discussed by Drs. McClanahan, Abt, La Fétra and Graham.

34. Dr. Thompson S. Westcott: "Pseudorubella in Infants."

The paper was discussed by Drs. Nicoll and Westcott.

35. Dr. Fritz B. Talbot: "The Energy Metabolism of a Cretin."

The paper was discussed by Drs. Sedgwick and Talbot.

36. Drs. George N. Acker and Joseph S. Wall: "Multiple Sclerosis in a Child of Four and One-half Years."

The paper was discussed by Dr. Wall.

37. Drs. Samuel S. Adams and Frank Leech: "The Dangers from Carriers of Diphtheria to Hospital Efficiency."

The paper was discussed by Drs. Graham, Gittings, Nicoll, Freeman and Adams.

The following papers were read by title:

1. Dr. Henry L. K. Shaw: "The Schick Reaction in Infants."

2. Dr. Walter Lester Carr: "Pneumonia at the Base of the Lung."

3. Dr. Langley Porter: "Study of a Case of Diabetes Insipidus."

4. Drs. H. J. Gerstenberger and H. O. Ruh: "Report of Clinical Results Obtained from Two Different Kinds of Milk."

Dr. Freeman expressed his thanks to Dr. Adams and the other members for their cooperation in making the meeting a success.

EXECUTIVE SESSION, MAY 10, 9 A. M.

The Report of the Council was read by the Chairman of the Council, Dr. L. E. La Fétra, as follows:

The excuse of Dr. Lucas for absence from the present meeting in order to organize the relief work for babies in Belgium was accepted.

The resignation of Dr. Wentworth was received, and it was recommended that it be accepted.

Dr. Dorning, on his request, was recommended for Emeritus membership.

The following nominations were submitted to the Society: For President, Dr. F. S. Churchill; for Vice President, Dr. Wilder Tileston; for Secretary, Dr. Howard C. Carpenter; for Treasurer, Dr. Charles Hunter Dunn; for Recorder-Editor, Dr. L. E. La Fétra; for Assistant Recorder-Editor, Dr. Oscar M. Schloss.

In connection with the retirement on his own request of our Secretary, who has completed twenty-four years of cheerful and faithful service for the Society, the Council with unanimity desires to express to Dr. Adams the sincere appreciation and thanks of the Society.

For the place and time of the next meeting the Council recommended White Sulphur Springs, May 29, 30 and 31, 1917, provided satisfactory arrangements can be made.

The Council reported that the Treasurer's Report had been received, audited and found correct.

The annual assessment for the ensuing year was fixed at $10.

The following names were recommended by the Society for election

to membership: Dr. Kenneth D. Blackfan, Baltimore; Dr. Frederic H. Bartlett, New York.

The amendment to Article XVI, Section 3, proposed in 1915, was carried, thus making the Section read as follows: "Papers shall not exceed fifteen minutes in the reading. In the discussion following the reading of such papers, remarks shall be limited to five minutes. Should any paper be too long to be read in fifteen minutes, the writer must prepare an abstract which can be read within that time."

Votes of thanks were given to: Dr. Rowland G. Freeman for his delightful entertainment of the Society at the Chevy Chase Club; to the New Willard Hotel for its courtesy, and to Dr. S. S. Adams for his faithful and cordial service as Secretary of the Society.

SAMUEL S. ADAMS, Secretary.
LINNÆUS E. LA FÉTRA, Recorder.

FRESH AIR IN PEDIATRIC PRACTICE

PRESIDENT'S ADDRESS

ROWLAND GODFREY FREEMAN, M.D.
NEW YORK

There is an agent of wonderful power and value to the pediatrician, the use and action of which is little appreciated even by the more prominent in the pediatric community. It has, therefore, seemed to me worth while to speak of its method of action and of its application to the uses of the pediatrician. I refer to fresh air.

By fresh air as a therapeutic agent I mean moving and cool outdoor air. The still air of the hot, humid dogdays of summer is little better than that of the crowded, hot room in winter. Fresh, moving, cool, outdoor air stimulates the appetite, induces quiet sleep, brings color to the cheeks, and increases the resistance of the organism to infection.

In seeking an explanation of the action of fresh air on the human body we find the claim that fresh, cold air raises materially the blood pressure. This claim, however, has not been confirmed by subsequent investigation, and we seem driven to the position that the favorable action of fresh air on the organism is due to the absence of the deteriorating effects of closed rooms. In fresh air the body has the advantage of normal conditions, while any modification of these, from a room with the windows partially open to a closed room, or to the conditions in the Black Hole of Calcutta, furnishes increasingly serious results from air stagnation.

The idea that air which had been breathed by other people was unhealthful probably arose from the unpleasant odor of closed and crowded rooms, and from symptoms elicited by extremes of this sort. The symptoms produced by closed places are depression, headache, dizziness, nausea, perspiration, thirst and difficult breathing. The elements producing these results were supposed to be a diminution of the oxygen and an increase of the carbon dioxid, with the possible appearance in such an atmosphere of a really poisonous product from the expired air. Experiments, however, have for the most part discredited this theory. The amount of oxygen in crowded, closed rooms is not depleted to a danger point, nor is the amount of carbon dioxid increased

to such a point. Efforts to find a poisonous element in such air have been made from time to time with negative results. In 1911 Rosenau and Amoss[1] carried out a series of experiments on guinea-pigs to demonstrate this, but subsequent work by Weisman failed to confirm their results, and Lee[2] states "that it may be regarded as finally settled that expired air contains no volatile, toxic, organic constituent."

In 1883 Hermans[3] of the Hygienic Institute in Amsterdam became convinced of the error of the oxygen and carbon dioxid theory, and found that his own temperature was raised in crowded assemblages from three-fifths to more than a degree Fahrenheit; he concluded that the discomfort of crowded places was due to inability of the body to cool itself in a hot, moist atmosphere.

Flugge's[4] experiments in 1905 really showed the condition that produced the symptoms elicited by enclosure. He put a subject in a closed box until symptoms appeared and then allowed him to breathe, through a tube, air from the outside, without any relief of his symptoms. Another subject, outside the box, on breathing the air from the inside had no symptoms. This showed that the discomfort of a closed place has nothing to do with the air we breathe, but with conditions of the skin brought about by such confinement. We suffer in crowded, unventilated places through lack of function of the skin, rather than through respiratory embarrassment. Recent experiments have demonstrated more directly the nature of this embarrassment, for if an electric fan is placed in the corner of the box and the air in the box is put in motion the symptoms disappear immediately.

These symptoms then are due to stagnant, hot, moist air surrounding the body. They may be produced in such an enclosed experimental box; they may be produced in an auditorium, overheated and crowded with people, or in a tightly closed living-room with few people, but no moving air, and such symptoms will be accentuated in people wearing heavy, impervious clothing that prevents access of moving air to the skin. It is evident, then, that we should wear as little clothing as is consistent with comfort. Most of us could wear much less clothing than we are accustomed to wearing.

The result of these elaborate observations is in brief that fresh air

1. Rosenau and Amoss: Jour. Med. Research, 1911, xxv, 35.
2. Lee: Jour. Am. Med. Assn., 1914, lxiii, 1625.
3. Hermans: Arch. f. Hyg., 1883, L, 1.
4. Flugge: Ztschr. f. Hyg., 1905, xlix, 363.

is good, not because it supplies oxygen, not because it is not overloaded with carbon dioxid, not because it contains no poisonous element, but because it allows the body to exist under such circumstances that it can control its moisture and temperature.

In the application of these newly developed facts to our daily work in pediatrics we have to combat the traditional fear of drafts and the habit of many people of living in close, hot rooms. It is only on account of the general acceptance of the brilliant results obtained in certain diseases, notably pneumonia and tuberculosis, by the use of fresh air, that we are able oftentimes to obtain the fresh air for our children which they need for the preservation of health and their proper development. Equally brilliant results possible in other diseases are not known by many physicians.

I believe that the cold air of winter is much more stimulating and produces better results in children than the mild air of spring and autumn.

Dr. Ellsworth Huntington of Yale,[5] in a very careful and interesting study of the influence of climate on civilization, concludes that spring and autumn are the periods of greatest mental and physical activity. This is contrary to the inferences I have drawn from my experiences with the influence of outdoor air and I find that his results are obtained from occupations which are housed during the winter, that is to say, college students, factory workers, etc. These people are all housed in winter and live in warm air and thus are little affected by the tonic action of cold outdoor air. In spring and autumn, on the other hand, the windows are opened. If he had used outdoor occupations for his studies I believe his results would have been different.

The best results from fresh air are obtained by keeping the children out of doors day and night, and we have no healthier children than those who, having suffered in early life from tuberculous infection, have been kept for years out of doors. These children are not subject to colds which others have during the winters; they have good color, good appetite and a normal, robust development.

Many of our pediatricians have confused fresh air with cold air, and one may see in hospitals cold wards and warm wards. Such cold wards are probably better than warm wards, but they lack altogether the free, moving air which is the great advantage of the outdoor ward.

5. Huntington, Ellsworth: Civilization and Climate, Yale University Press, 1915.

aud often the sunshine, which we know to be one of the most potent of our therapeutic agents.

Outdoor sleeping porches enclosed on three sides and roofed, but open to the south, furnish the best fresh air at night, while in the daytime balconies and rooms without heat and windows wide open supply the air we need.

It is evidently not enough, however, that we should have this fresh air, but we should also look to the clothing to see that our children are not sealed in with heavy, impervious covering so that the skin is unable to rid itself of the heat and moisture.

The experiments I have reviewed show us how it might not be impossible for a child out of doors, in cold weather, to be embarrassed by such clothing.

Where it is impossible to obtain such complete outdoor exposure, the best substitute in cold weather has seemed to me to be in rooms with cheesecloth screens in the windows. Such cheesecloth screens should cover all the space available when the windows are opened. They allow a moderate access of air without the presence of the much-feared drafts. The objection is that they allow less sunlight than glass, but this disadvantage is more than counteracted by the quality of the air of the room.

Other methods of ventilation consist in patent ventilators put under the lower sash. These, however, allow more movement in the air of the room, but less open space, and some of them furnish no filtration of the dust from the air.

The greatest blight on the fresh air movement of the day is the vogue of elaborate, mechanical ventilating systems, which obtain the air from the basement, pump it through flues into and out of the rooms. Such systems are very expensive, occupy a great deal of space, and while the air furnished may be sufficient for the preservation of life, it often lacks the freshness and invigorating character of the air obtained from open windows or through cheesecloth screens. The worst phase of the current ventilating systems is when they prohibit the opening of the windows. Under intelligent operation they may prove efficient. Closed rooms favor the conveyance of disease from one person to another, and our ventilating systems make practically no provision for carrying off germ-laden dust. There is little conveyance of disease in outdoor school classes or outdoor hospital wards.

The danger of housing is not alone in the bad air of a closed room, but to a susceptible organism it consists also in the sudden change from a temperature of 70 or 80 in a dry room all night to a temperature perhaps of zero, with a cold north wind blowing out of doors, then to a heated auditorium, with a saturated, moist temperature of 80, and again out into zero weather. It is only during the existence of marked changes of temperature between indoors and outdoors that epidemics of colds exist, for during the summer we have practically an immunity to colds and colds occur only when our houses are closed.

In New York our epidemics of colds usually begin in November and December, while in New Hampshire, where I often spend my summers, cold weather inducing people to heat their houses often occurs in September, and it is not uncommon for the neighboring town to have a severe epidemic of colds at such a time. In the summer time the air is less invigorating, but there is the advantage of less sudden change from cold to hot or from dry to moist air.

Much is heard of the superiority of country air over city air, but recent investigations have shown but little difference in its chemical composition, and if the children are kept in the open air, as they should be in the city, they are much healthier than most country children.

Night outdoor air, while it is not so good as day air because it lacks the beneficent effect of sunlight, is far superior to night air in the house, and the advantage of fresh air treatment is reduced by half if children are housed at night.

A statement as to the diseases to which fresh air treatment is applicable is much more difficult than a statement of the diseases to which it is not applicable. I will, therefore, first enumerate the conditions to which fresh, cold air has not been demonstrated as practicable.

Premature infants who show a subnormal temperature in cool air should be kept at an air temperature that will preserve the normal body temperature. This warm air, however, must be a freely moving warm air, rather than the dead air found at the bottom of a box. On this account, for such babies, a properly constructed incubator is far superior to the substitutes that are often adopted.

I am not sure whether such cold, fresh-air treatment is applicable to children with kidney lesions or with severe heart lesions, although I have seen children with severe endocarditis who preferred to be out

of doors in winter rather than in closed rooms, and I have seen no injury from such exposure.

The most important application of this fresh-air treatment is to build up the vitality and resistance to disease of frail children, and in this sphere, I think, it shows perhaps its most brilliant results. This is true in early life, for children with marasmus and malnutrition who are impossible to feed so as to obtain an increase in weight will often gain promptly, with no change in food, on being kept out of doors or in front of an open window in winter. I have seen many children who have reached that stage of malnutrition that usually precedes death, with a dusky hue of the face, react to such treatment and recover entirely.

Another condition of early life, rachitis, is, I believe, entirely a disease of housing. It exists, not in tropical climates where people live out of doors, but in colder climates where people house themselves in winter. The symptoms develop in winter only and the severe cases that we see are entirely confined to the children of races that have been accustomed to warm climates where the families do not house themselves in winter. This susceptibility is not confined to human beings, but exists equally in the lower animals. Animals brought here from tropical climates develop a disease that is in many respects similar to our rachitis and which is known in zoological gardens as cage-disease, and this is the fatal disease that all zoological gardens have to combat and from which none will be free until greater care is taken to supply these animals with fresh, cool, moving air in winter. On account of this susceptibility Italians and colored people and other people accustomed to tropical climates should be warned that they must give their children fresh air in winter if they would have them survive and develop properly.

In all the acute infectious diseases I think there is now a general acceptance of the advantage of fresh air, excepting perhaps in measles and scarlet fever. In tuberculosis there is now no question of its advantage. In pneumonia the results from this treatment have exceeded those from any other method of treatment, including specific treatment with serums and vaccines. There are still many men, however, who, while allowing that fresh air is beneficial in an inflammation of the lung, doubt its efficacy in bronchitis, pharyngitis, laryngitis, rhinitis and otitis. The only reason why such men doubt its efficacy is because they have not sufficiently tried it. I have used it in all these

conditions and I believe that it is of direct benefit and that it diminishes materially the mortality.

I have convinced myself also that measles and scarlet fever are no exceptions to the rule, and I have put patients during a severe measles epidemic complicating scarlet fever out of doors in winter without a single fatality, although some of the scarlet fever patients were exceedingly sick when the change was made. The change to outdoor air seemed to help them all. Among these cases was one of scarlet fever in which from a breaking down of the lymph nodes there was a large ulcer extending from one side of the neck to the other. Under the influence of the cold air the neck healed with a linear scar. It is equally unnecessary in measles to darken the room. We should let children with this disease have all the sunlight that their eyes will bear, as well as cold, fresh air.

In connection with the healing of this surgical condition complicating scarlet fever, the statements made by H. S. Soutter[6] are of interest. He says that they received wounds that were soiled by earth, manure and fragments of cloth covered with mud and that there was one way by which all such infections might be defeated, by plenty of fresh air or oxygen. In several cases, in which the wounds were so horribly foul that it was impossible to tolerate them in the wards, the patient was put in the open air with the wounds covered only by a thin piece of gauze. The results were almost magical. The wounds lost their odor and began to look clean, while the patient lost all signs of the poisoning which had been so marked before. He thinks this treatment may account for the fact that they had no case of tetanus.

J. W. Markoe states his experience with open-air treatment in sepsis at the Lying-In Hospital in New York. Of fifty-seven patients treated indoors, two left the hospital and fifty-five died; that is, all the patients who remained in the hospital died; while of fifty-three patients who were put out of doors, twenty-two, or 41 per cent., recovered.

The common colds of winter are favorably influenced by cold, fresh air, as are other forms of infections.

In diseases characterized by abnormal conditions in the blood, such as simple anemia, von Jaksch's anemia and leukemia, I believe there is a large field of usefulness for this treatment, and I have myself, in a very limited number of cases, obtained quite brilliant results.[7] These

6. Soutter, H. S.: A Surgeon in Belgium, 1915.
7. Freeman, R. G.: Am. Jour. Med. Sc., 1916, cli, 1.

observations must, however, be confirmed by many more before one can consider this claim as proved. Markoe, however, states that patients with anemia from severe hemorrhage are greatly benefited by fresh air.

Before closing, it would seem that some explanation is due as to why, if all these statements are true, children are still housed and many adults have a panic if a breath of cold air strikes the back of their necks or their bald heads, while children who are brought up without fear of cold enjoy it wherever it strikes.

The supposed production of catarrhal inflammations in adults by exposure to cold air, if it really exists, exists only on account of suggestion. These people have been brought up to such a fear of fresh air that every infection of the upper air passages to which they succumb they attribute to this health-giving influence. It is sincerely to be hoped that many of the coming generation may be brought up under different ideas and may be less dependent on hot, offensive, stagnant air for the supposed comforts of life.

There is evidence enough to show that many diseases are favorably influenced by this simple and safe measure. Why do you not use it? Some are afaid, some will not take the trouble. Many children are allowed to become sick from housing and children may be seen dying in closed wards of many of our best hospitals who might have been saved had they been put out of doors.

211 West Fifty-Seventh Street.

RECENT PROGRESS IN OUR KNOWLEDGE OF THE PHYSIOLOGIC ACTION OF ATMOSPHERIC CONDITIONS

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Two weeks ago today, in the physiologic laboratory of the Columbia School of Medicine, Dr. Fred W. Eastman and I made the following experiment: A young man, 21 years of age, in excellent physical condition, who was willing to act as the subject of our tests, was dressed in light underclothing and light trousers, a sweater, stockings and shoes. His systolic and diastolic blood pressures and his pulse rate were taken in the sitting posture; the carbon dioxid content of the alveolar air of his lungs was determined; a pneumograph was attached to his chest for recording his respiratory movements; a resistance thermometer was placed in the rectum and connected with a self-writing galvanometer for the continued record of his bodily temperature; and a flat-bulbed thermometer was strapped firmly to his forehead to serve as an indicator of the temperature of his skin. Thus equipped he entered a small chamber, provided with a door and windows and with facilities for heating and humidifying the air. He remained there, sitting quietly, for a period of four and one quarter hours. The temperature of the air in the chamber was raised as quickly as possible above the temperature of his body and reached a maximum of 43.3° C. (110° F.) with a maximum wet-bulb reading of 37.2° C. (99° F.), while the relative humidity was increased to a maximum of 85 per cent. For a period of two and one quarter hours the door of the chamber was kept closed, although it was not wholly air-tight, and the unusual atmospheric conditions were maintained, although not continually at their maximum. Afterward the door of the chamber was opened and the air within was allowed to acquire the more comfortable conditions of the room air outside, which possessed a temperature of 18° C. (64.5° F.) and a relative humidity of 51 per cent. During the whole time of the experiment a continuous record was made of the subject's bodily temperature; at intervals of fifteen minutes measurements

were made of the temperature and the humidity of the air of the chamber, of the temperature of the subject's mouth and of the skin of his forehead, and of the rate of his pulse and his respiration; at intervals of every hour his systolic and diastolic blood pressures and the carbon dioxid content of his alveolar air were determined; while occasional records were made of the carbon dioxid content of the air of the chamber and of the subject's sensations. The results of the experiment will be discussed later. It is typical of many experiments, similar in object, although differing in details, which have been performed in recent years inside and outside many laboratories in an endeavor to discover the relations of the individual to the air that surrounds him.

As one result of these experiments there has been a great change in our ideas concerning the physiologic action of atmospheric conditions. It had long been the custom to ascribe to chemical components of the atmosphere the bad effects of living in air that had already been breathed by human beings. The discovery of oxygen and of carbon dioxid early in the last century gave a great stimulus to this notion, and it became firmly fixed in the minds of chemists, physiologists and physicians, as well as the educated masses, that air that had been breathed was vitiated chemically and rendered unfit for human use by the lack of oxygen, the accumulation of carbon dioxid and the presence of an organic poison of unknown nature. No sooner had this notion become widely accepted than the laboratories began to demonstrate the inadequacy of the supposed proof of the notion, and, to cut a long story short, we now know that, except under very unusual circumstances, the harmfulness of respired air is not due to its chemical components. By respiration oxygen cannot be reduced to a deleterious proportion nor can carbon dioxid be produced in deleterious quantity, except under very unusual conditions of living; and the organic poison of respiration has no real existence. The harmfulness of living in confined air is found in certain physical rather than chemical features; the air is too warm, too moist, and too still; and if it has not these physical features it is not harmful.

We all have sat in crowded assemblies; we all have experienced the hot, humid, still days of an American summer. We all know the effects of such air on our sensations, the general bodily discomfort, the sleepiness, the flushed face, the headache, the disinclination to think or to act, the general debility, the longing for relief. But sensations are an inadequate measure of bodily conditions. In what respects is hot,

humid, still air harmful? To answer this question we must consult the records of many researches, chiefly on human beings, but partly on animals, that have been undertaken since Hermans,[1] more than thirty years ago, observed that in crowded theaters and churches his own bodily temperature rose. The most recent of these researches is that of the New York State Commission on Ventilation,[2] which has been in progress for the past two and one-half years and is not yet completed.

Notwithstanding that man is supposed to be a homothermal organism, there is a certain relationship between his bodily temperature and the temperature of his environment, even under the ordinary conditions of living. This has been shown by the New York Commission, which found that during the months of June and July the rectal temperature of its subjects at 8 a. m., living in their own homes, was conditioned by the average atmospheric temperature of the preceding night. If the night had been warm the bodily temperature in the morning was high; if cool, the bodily temperature was low. The variation of bodily temperature was about 0.55 degree C. (1 degree F.) for 20 degrees of atmospheric temperature, although it is probable that the degree of variation can be modified by the clothing. The commission further found that, whatever the bodily temperature of its subjects might be at the beginning of an experiment, it was lowered by confinement in an atmosphere of 20° C. (68° F.) and 50 per cent. relative humidity, and raised by confinement at 23.9° C. (75° F.) with the same humidity, or still more by 30° C. (86° F.) with 80 per cent. humidity. The final average bodily temperatures in certain series of observations, where the subjects were confined in the observation chamber for from four to seven hours were as follows:

After 20° C. (68° F.), 50 per cent. humidity, the average bodily temperature was 36.7° C. (98° F.).

After 23.9° C. (75° F.), 50 per cent. humidity, the average bodily temperature was 36.9° C. (98.5° F.).

After 30° C. (86° F.), 80 per cent. humidity, the average bodily temperature was 37.4° C. (99.3° F.).

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1. Hermans: Arch. f. Hyg., 1883, i, 1.

2. Members of the New York State Commission on Ventilation are C.-E. A. Winslow (chairman), D. D. Kimball, Frederic S. Lee, J. A. Miller, Earle B. Phelps, E. L. Thorndike, and G. T. Palmer (chief of investigating staff). The results of their investigations have as yet been published only in part. For a general presentation of some of the results see Am. Jour. Pub. Health, 1915, v, 85.

Haldane[3] and others have shown a greater elevation of bodily temperature in more extreme atmospheric conditions, and have pointed out the accompanying dangers of heat stroke. Eastman and I have seen the temperature of a normal adult man rise 3.3° C. (6° F.) during a stay of three and one-quarter hours in an atmosphere averaging 40.4° C. (104.7° F.) in temperature and 95 per cent. in relative humidity. The relation between bodily temperature and external cold has not been so fully studied, but enough is known to warrant the statement that, in normal individuals at least, the bodily temperature can be to a considerable degree controlled by controlling the temperature and the humidity of the surrounding air. It is altogether probable that the same is largely true in febrile diseases.

External temperature exerts likewise a definite effect on the circulatory system. The rate of the heart beat is increased in warm, humid, and decreased in cool, dry air. The New York Commission found the average rate of its subjects confined in an atmosphere of 30° C. (86° F.) and 80 per cent. relative humidity to be 74, and in an atmosphere of 20° C. (68° F.) and 50 per cent. humidity to be 66. Eastman and I have seen the pulse rate increase by 39, from 67 to 106, as the temperature of the air surrounding the subject rose from 23.3° to 43.3° C. (74° to 110° F.) and the humidity from 58 to 90 per cent.

The important and involved topic of the relation of atmospheric conditions to blood pressure I must leave until the abundant data that have been accumulated by the New York Commission have been subjected to a more careful examination than has yet been possible, although it may be said that excessively high temperatures and high humidities are accompanied by an elevation of both systolic and diastolic pressures. A study of the Commission's records by one of the various methods for evaluating vascular data seems to reveal another fact of distinct importance. When the human body rises from a recumbent to a vertical position the threatened settling of the blood into the lower parts by gravity, with the resultant deleterious effects, ought obviously to be counteracted. In the healthy person the most expedient way to accomplish this is by means of a vigorous vasomotor mechanism acting to constrict the arterioles and raise the blood pressure. This mechanism is assisted by a quickening of the rate of the

3. Haldane: Jour. Hyg., 1905, v, 494. Haldane, Pembrey, Collis, Boycott and Cadman: Rep. Dept. Com. on Humidity and Ventilation in Cotton Weaving Sheds, London, 1909 and 1911.

heart's beat. If the mechanism be enfeebled from any cause, there may be, along with the change of posture, a lessened rise of blood pressure, or even a fall, and a great increase in the heart rate. A comparison, therefore, of the change in the systolic blood pressure and the change in the rate of the pulse resulting from a change of the position of the body from the horizontal to the vertical gives a clue to the efficiency of the vasomotor mechanism. On this basis Crampton[4] has constructed a scale of percentages of vasotone. In terms of this scale the New York Commission finds that the vasotone diminishes in hot and humid air, and increases as the air becomes cooler and dryer. Thus these results indicate that a distinct vascular benefit follows from exposing the body to a cool dry air.

Atmospheric conditions exert on the respiratory system effects of various kinds. On the rate of respiration a moderate degree of heat and humidity seems to be without effect, but more extreme conditions cause a quickening of the breathing, and this is probably accompanied by more shallow respirations. The more extreme conditions too appear to result in a lowered concentration of carbon dioxid in the air of the pulmonary alveoli, although I cannot yet quote actual figures to demonstrate this. The matter, however, is important, since a lowered alveolar carbon dioxid may signify an increased content of hydrogen ions, in other words, increased acidity, in the blood. Eastman and I are now investigating this point with much interest.

The mucous membrane of the respiratory tract is markedly affected by atmospheric conditions. This was shown three years ago by Hill and Meucke,[5] and it has recently been quite fully investigated by Miller and Cocks[6] under the auspices of the New York Commission. Exposure to heat causes increased swelling, redness and secretion in the nasal mucosa, and these effects are more marked when the humidity of the air is high. Exposure to cold reverses the effects. When the subject passes from a cool to a hot room and a current of air is played upon the face there occurs a diminution of the swelling and the secretion; but passage from a hot to a cool room with a similar draught results in increased swelling and increased secretion. This latter condition seems to be especially favorable for the development of infectious microorganisms. But the causative relation of the bacteria of the nasal mucosa to "colds" seems to be still in doubt.

4. Crampton: New York Med. Jour., 1913, 98, 916.
5. Hill and Meucke: Lancet, London, 1913, 1291.
6. Miller and Cocks: Tr. Am. Climatol. and Clin. Assn., 1915.

The distaste for physical labor which we feel on a hot humid day is a common experience, and it is often interpreted as real inability to work. The New York Commission found, in their experiments with human beings, that, if pushed, the individual is capable of performing as much muscular work in an atmosphere of 30° C. (86° F.) and 80 per cent. relative humidity as in one of 20° C. (68° F.) and 50 per cent. humidity, but that he is not inclined to do so much. The lack of exact knowledge as to what the muscles themselves, apart from the nervous system, can do under such circumstances induced Scott and myself[7] to investigate the subject on animals. Taking the comfortable condition of 20.6° C. (69° F.) with 52 per cent. relative humidity as our standard, we found that when cats were confined for six hours in a well-ventilated chamber, the air of which was kept at an average temperature of 32.8° C. (91° F.) and with an average humidity of 90 per cent., the excised muscles of the animals lost in the length of their working period before exhaustion 11 per cent., and in the total amount of work which they were able to perform 24 per cent. At an intermediate temperature and humidity they lost in an intermediate degree. These results indicate that the distaste for physical labor which is felt on a hot and humid day has a deeper basis than mere inclination; the muscles themselves are actually incapable of performing as much work. We found, moreover, that in the extreme condition the blood lost as much as 6 per cent. of its sugar, and 2 per cent. when the intermediate condition was maintained. There is evidently correlation between decreased blood sugar and decreased muscular power, and we have suggested that a physiologic adaptation is here indicated, such that "when it is physiologically fitting that the animal reduce muscular exertion to a minimum, in order that the output of heat may be as low as possible, as in a hot and humid environment, the supply of fuel will be lowered correspondingly."

Little can be said at present regarding the action of atmospheric conditions on the nervous system. The rise of external temperature by dilating the cutaneous blood vessels undoubtedly makes the brain anemic, but it is not certain that variations in such temperature with or without variations in humidity markedly affect the action of the nerve tissues, unless the variations are excessive. The New York Commission, under the lead of Thorndike, has expended much time and effort in endeavors to detect a possible influence of atmospheric variations between moderate limits on the ability to do mental work. The subjects

7. Lee and Scott: Am. Jour. Physiol., 1916, xl, 486.

were given such psychologic tests as cancelling arithmetical figures, adding figures, mentally multiplying three-place by three-place figures, typewriting, and more complex mental performances which involve choice and judgment. The range of atmospheric variation was from a lower limit of 20° C. (68° F.) and 50 per cent. relative humidity to an upper limit of 30° C. (86° F.) and 80 per cent. humidity. In some cases the air was quiet, in others it was kept in motion by electric fans. The tests continued for periods of from 4 to 7 hours and in some cases they were repeated for 6 successive days under the same conditions. In neither the young men nor the young women subjects of these tests could there be detected any relation between atmospheric conditions and either the accuracy or the amount of the mental work that was performed. A series of experiments on a larger scale has been instituted, but is not yet completed.

The relation between atmospheric conditions and metabolic phenomena is not yet elucidated. During the summer of 1914 the New York Commission made a partial study of this topic on human beings with the assistance of Mr. H. L. Higgins, then of the Carnegie Nutrition Laboratory. The terms employed included such subjects as total metabolism or total heat production, the metabolism of carbohydrate, and the metabolism of protein. The results were almost wholly negative. They cannot, however, be regarded as conclusive. As regards lesser specific changes in metabolic processes, too, little can be said at present. But the facts that external cold increases metabolism, that profound metabolic changes occur in the fevers of infection and that there is some evidence that in hyperthermy produced in other ways than by infections metabolism is altered, lead us to suspect that it may be changed, not only totally but in specific details, with even moderate changes in the surrounding atmosphere. It is difficult to believe that a relationship that is so amply demonstrated for the physical phenomena of the body does not involve also its chemical performances.

A further topic that is inviting is the possible relationship between atmospheric conditions and bacterial infections. Most of the experimental observations that have here been made relate especially to the action of temperature on the course of infections, and it has generally been found that high external temperature with accompanying pronounced increase of bodily temperature checks the progress of infections that are already existing. Somewhat lower temperatures, 30° to 35° C. (86° to 95° F.), on the other hand, seem to favor the multi-

plication of the bacteria and the advance of the disease. In the experiments of Winslow, Miller and Noble[8] of the New York Commission, in which rabbits were confined in air of from 29° to 32° C. (84.2° to 89.6° F.) there was, in the first three weeks, a distinct decrease in the formation of hemolysins when the animals were compared with control animals kept at lower room temperatures. Similar but less striking results were obtained in the formation of agglutinins.[9] It thus appears that external temperatures up to about 30 C. (86 F.) are unfavorable to the development of immune bodies in the blood. Miller and Noble[10] found, furthermore, that respiratory infections of rabbits with *Bacillus bovisepticum* (snuffles) is favored by the chilling of such animals after they have been accustomed to heat, and some of their results suggest that a change from a low to a high external temperature also predisposes to similar infection. Although Chodounsky[11] obtained only negative results, the weight of the recent experimental evidence favors the view that the exposure of the body to cold is favorable to the incidence of acute respiratory disease, and it appears not improbable that the primary seat of this deleterious influence is in the mucous membrane of the upper air passages.

No review of recent progress in our knowledge of the relation of man to the atmosphere would be complete if it failed to take note of the striking observations of Mr. Ellsworth Huntington,[12] which are set forth in his engaging book. Mr. Huntington made a careful study of the output of industrial workers in various factories in the state of Connecticut, as determined by their monthly wages for piece work, over a period of four years. He found that the annual course of production was as follows: Low at the beginning of the calendar year, it fell still lower and reached its minimum at about the end of January; through the spring there was a gradual increase in output until June; then a moderate decrease until the end of July; in the autumn an increase to the maximum in November; and then the winter descent to the succeeding January minimum. Production was thus greatest in the spring

8. Winslow, Miller and Noble: Proc. Soc. Exper. Biol. and Med., 1916, xiii, 93.

9. Winslow, Miller and Noble: Proc. Soc. Exper. Biol. and Med., 1916, xiii, 194.

10. Miller and Noble: The Effects of Exposure to Cold upon Experimental Infection of the Respiratory Tract, Jour. of Exper. Med., 1916, xxiv, 223.

11. Chodounsky: Erkältung und Erkältungskrankheiten. Wien., 1907.

12. Huntington: Civilization and Climate. New Haven, 1915.

and the autumn, and least in the winter and the summer. A very similar course was followed by the workers engaged in making electrical apparatus in Pittsburgh; and similar confirmation of the validity of the conclusions, with changes in details, was made by the output of other industrial workers in the southern states and by strength-tests of school children in Denmark. All these data combine to demonstrate that the greatest physical efficiency of the individual is found not during the summer or the winter, but at intermediate seasons. That the same is true also of mental activity is shown by a study of the marks secured by the students at West Point and Annapolis in certain classes, especially mathematics. Of the various climatic features of the different seasons that might be responsible for these seasonal differences in achievement, temperature appears to be the most important. Both physical and mental activity seems to be greatest and most effective, not when extreme summer's heat or extreme winter's cold prevails, but when the body is subjected to an intermediate temperature. After a careful consideration of his many figures Huntington came to the conclusion that the optimum temperature of the outside air for the physical work of human beings is about 60° F. (15.6° C.), and for the mental work about 40° F. (4.4° C.), the greatest total efficiency of the human body culminating at the intermediate point of 50° F. (10° C.).

We have thus seen that the body reacts to changes in atmospheric conditions in manifold ways. The most potent of the atmospheric agencies is undoubtedly temperature, but high temperatures exert greater effects when they are accompanied by high humidity. I have said little of the movement of air, but it should be understood that movement is an important agency, and its share in the physiologic phenomena has been studied by the New York Commission. By way of general summary it may be said that when an existing external temperature is fairly comfortable to the individual an elevation of it, especially when such elevation is accompanied by an increase of humidity, is deleterious, and the deleterious effects are more pronounced when the air is stagnant. Deleterious effects resulting from such a combination of atmospheric conditions may be in some degree obviated if the air next the skin be put into motion, but a more effective antidote is a reduction in the temperature of the air, and this may be assisted by a reduction in its humidity. All experimentation and observation go to demonstrate that a moderately cool and moderately dry air in motion constitutes the most physio-

logically helpful aerial envelope of the body. The customary figure of 70° F. (approximately 21° C.) for the atmosphere in which most persons engage in the ordinary occupations of the living room of a dwelling is too high; a range from 64° to 68° F. (approximately 18° to 20° C.), with not over 50 per cent. relative humidity, is undoubtedly better, but even such temperatures are too high when much physical activity occurs. Depending on activity and on more obscure corporeal conditions the same external temperature may feel at one time warm and at another time cold. The degree of comfort that is felt, which should not be allowed too potent an influence in deciding what one's environmental conditions shall be, depends, moreover, largely on the thickness of the clothing and on habit. It is surprising how readily one's habits in this respect may be altered. Uniformity in conditions should be avoided; too long a continuance of an existing temperature is dulling to the body; there should be not infrequent and marked changes. Artificial ventilating systems should not necessarily be condemned, but should be operated intelligently and may advantageously be combined with window ventilation.

In these days we hear much of "fresh" air and its merits. We have fresh-air funds, fresh-air schools, and fresh-air babies. All are commendable; but while giving to our funds, opening our schools, and putting our babies out of doors, let us clearly understand what constitutes fresh air. The freshness of so-called "fresh" air lies, not in more oxygen, less carbon dioxid, less organic matter of respiratory origin, and the hypothetical presence of a hypothetically stimulating ozone, but rather in a low temperature, a low humidity, and motion. So far as fresh air itself is concerned, there seems to be nothing more mysterious about it than this.

To what extent ought fresh air to be used as a therapeutic agent? Here intelligent experience, and not opinion without experience, is the only guide. That a physician, indeed, should have any article in his creed of therapeutics that is not based on the intelligent experience of somebody is not to be supposed. It cannot be denied that where intelligent experience has been applied to the topic of fresh air as a therapeutic agent the use of fresh air has been almost invariably extended. But no one has a right to maintain, therefore, that it is a panacea. Only when it has been tested in a great variety of pathologic conditions, and this can be done with entire safety to the patient, will the therapeutic use and limitations of this physiologically significant agent become known.

PYELITIS OF INFANCY

I. MODE OF INFECTION *

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There have been two antagonistic theories advanced to explain the mode of the infection of the kidney in pyelitis of infancy. One theory maintains that the infection of the kidney takes place by the ascending route, through urethra, bladder and ureters; the other, that the infection comes by means of the blood and lymphatics. Before discussing the relative merits of these two theories certain facts in regard to pyelitis as it occurs in infants need to be noted. The disease is much more common in girl than in boy infants, the proportion being nearly three to one. The organism most frequently causing the disease is the colon bacillus, which is the offender in from 50 to 90 per cent. of cases. The pathology of the condition is well established. In uncomplicated cases the pelvis of the kidney is the only portion of the urinary tract involved, and there the local lesion is simply a low grade inflammation. The ureters and bladder are normal. Many cases show in addition some degenerative changes in the kidney substance, due to extension of the process inward from the pelvis. When the tissues are invaded by pus-forming cocci, there is secondary abscess formation.

With these facts as a basis, those who believe in the ascending route of infection argue that the colon bacillus enters the urethra, ascends against the urinary stream and, causing no lesions in its progress, localizes in the pelvis of the kidney and by its growth there gives rise to disease. This theory gains its greatest support from the large proportion of cases among girls, who, theoretically with a short urethra and of easy contamination with fecal matter, become more readily infected. There is very little experimental work in its support. Bond[1] showed that in the intestine, fallopian tubes and biliary passages solid particles may be carried upward by a current hugging close to the surface, and that in the ureter, when no urine is coming down, this

* From the Children's Medical Department, Massachusetts General Hospital.

1. Bond: Med. Rec., New York, 1905, lxviii, 246.

passage upward may also occur. Many others[2] state the opinion that ascending infection may occur in some or all cases, but they have no sure evidence to support the belief.

Directly against the ascending method of infection are the facts that colon bacilli have never been shown to pass up the normal, unobstructed ureter and that the colon and tubercle bacilli have been introduced repeatedly into the bladder and in the presence of a normal mucous membrane are excreted without causing damage of any kind.[3] Ascending infection occurs only in the presence of obstruction to the outflow of urine and cannot occur if the sphincter of the ureter is normal.[4] It seems to me that the ascending theory of kidney infection so far as it applies to the pyelitis of infancy has not been proved and the facts are against it.

The theory of kidney infection by the blood and lymphatics rests upon much surer ground. The work of Thiele and Embleton[5] seems to show that bacteria may pass to the kidney by the lymphatics alone, appearing first in the fat capsule and being distributed through the kidney also by the lymphatics. If bacteria appear in the urine, that is, if they have passed through the kidney, they must have reached the kidney by the blood stream. This latter procedure is what occurs in pyelitis, so we must have had a blood infection.

The direct lymphatic connection as shown by Franke[6] between the

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2. Among these may be cited the following:
Thomas, J.: Lancet, London, 1913, ii, 467.
Wright: Practitioner, London, 1909, lxxxii, 344.
McCrea: Practitioner, 1910, lxxxv, 346.
Wyman: Boston Med. and Surg. Jour., 1914, clxx, 540.
Freeman: Jour. Am. Med. Assn., 1914, lxiii, 1802.
Cunningham: Jour. Am. Med. Assn., 1915, lxiv, 231.
Heubner: Jahrb. f. Kinderh., 1913, lxxvii, 1.
Ross: Lancet, London, 1915, i, 654.
Shaw: Clin. Jour., 1908, xxxi, 273.
Box: Brit. Med. Jour., 1910, ii, 1128.
Barnard: Lancet, London, 1905, ii, 1243.
Herringham: Clin. Jour., 1909-1910, xxxv, 241.
Sampson: Bull. Johns Hopkins Hosp., 1903, xiv, 334.

3. Leutscher: Bull. Johns Hopkins Hosp., 1911, xxii, 361. Bauereisen: Ztschr. f. gynäk. Urol., 1910, ii, 132.

4. Rovsing: Sixteenth International Medical Congress, Budapest, 1909.

5. Thiele and Embleton: Proc. Roy. Soc. Med., Path. Sec., 1913-1914, vii, 69.

6. Franke: Mitt. a. d. grenzgeb. d. Med. u. Chir., 1911, xxii, 623; Ibid., 1911, xlviii, 1973.

colon and the right kidney, which is the kidney most frequently affected in unilateral infection, has led some writers[7] to believe that bacteria pass directly from the intestine to the kidney by these lymph vessels — the so-called transparietal route. This probably occurs, but gives rise to an infected kidney, not to pyelitis as we see it in infants. Pyelitis may follow this condition by secondary blood infection.

The usual mode of infection in pyelitis appears to be somewhat as follows: From the intestinal tract or some other source bacteria get into the lymphatic vessels and then into the blood, or possibly directly into the blood. They are transferred by the blood to the kidney. After reaching the kidney they pass through the glomeruli and are excreted at the pelvis. They may pass out of the body in the urine without doing any damage, or they may set up an infection at their point of excretion, that is, produce a pyelitis. They may during their passage through the kidney cause more or less damage to the various portions of the organ. Which of the alternatives occurs within the kidney depends on the virulence and character of the bacteria and on the resistance of the individual and of the local tissues. The colon bacillus, being of comparatively low pathogenicity, causes almost no damage to the kidney substance in its passage through the organ. An infection of the kidney may take place by extension inward from the pelvis, probably by lymphatic channels. This infection causes a greater or less degree of permanent damage to the substance of the kidney and presents a complication of, or sequel to, the usual pathology of the disease. The various stages in this process as outlined in the foregoing statement have been well established.

Blood infection in nearly all the acute infectious diseases is now so well known that no proof needs to be given in its support. The colon bacillus has been found in the blood by several investigators.[8] Crabtree found that organism in the blood in seven out of nine patients who developed pyelitis under observation. The blood infection was always early in the disease, disappearing later, as in typhoid fever.

The intestinal tract is the most likely source of the infection in the majority of cases of pyelitis, especially in those due to the colon

7. Wilson: Brit. Jour. Child. Dis., 1913, x, 289. Jeffrey: Quart. Jour. Med., 1910-1911, iv, 267.

8. Crabtree: Lancet-Clinic, 1916, cxv, 96. Moser: Deutsch. Ztschr. f. Chir., 1915, cxxxii, 71. Ruediger: Philippine Jour. Sc., 1915, x, 25.

bacillus. Calmette[9] and many others[10] have shown that pigment particles, tubercle bacilli and other bacteria are carried with the fat from the intestinal canal in the lymph vessels of the mesentery during digestion and are distributed by the blood to all parts of the body, including the kidney. Other writers have called attention to the passage of the colon bacillus through the damaged intestinal mucous membrane,[11] and to the frequent association of pyelitis with constipation and other digestive disturbances.[12] Ten Broeck[13] found organisms of the colon bacillus group post mortem in the heart's blood of five out of fourteen patients dying of infectious diarrhea and in the ileocecal lymph nodes in five cases. Trumpp[14] found colon bacilli in the urine of fourteen out of seventeen children with follicular enteritis. Morse[15] and Knox[16] include cases of pyelitis in their reports of urinary analyses in gastro-intestinal diseases. Kowitz[17] has emphasized the seasonal incidence of pyelitis following the diarrheas of summer. Edith Williams[18] found in urine cultures of seventy consecutive cases that of forty-four patients with chronic intestinal disorders, sixteen showed colon bacilli. The importance of considering the gastro-intestinal tract in the treat-

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9. Calmette: Ann. de l'Inst. Pasteur, 1905, xix, 601; Ibid., 1906, xx, 353, 609; Compt. rend Soc. de biol., 1906, lxi, 161, 548.

10. Among these may be cited the following:
Arbeiter: Virchows Arch. f. path. Anat., 1910, cc, 321.
Whitla and Symmers: Brit. Med. Jour., 1908, ii, 61.
Nichols: Jour. Med. Research, 1904, xii, 455.
Ford: Tr. Assn. Am. Phys., 1900, xv, 389.
Adami: Montreal Med. Jour., 1898, xxvii, 485; 1902, xxxi, 105.
Cobbett: Jour. Path. and Bacteriol., 1910, xiv, 563.
Griffith: Royal Commission on Tuberculosis, Second International Report, 1907, Appendix 1, 628, 696.
Ravenel: Jour. Med. Research, 1903, x, 460.
Ravenel and Reichel: Jour. Med. Research, 1908, xviii, 1.

11. Park: Tr. Am. Surg. Assn., 1893, xi, 213. French: Brit. Med. Jour., 1908, i, 1029. Thiemich: Jahrb. f. Kinderh., 1910, lxxii, 243.

12. Brennemann: Jour. Am. Med. Assn., 1911, lxi, 631. Friedenwald: Arch. Pediat., 1910, xxvii, 801. Dudgeon: Lancet, London, 1908, i, 615. Green: Boston Med. and Surg. Jour., 1913, clxviii, 645. Cannato and Caronia: Pediatria, 1914, xxii, No. 9. Langstein: Med. Klin., 1913, ix, 1491. Zobel: Jour. Am. Med. Assn., 1916, lxvi, 496. White, W. H.: Lancet, London, 1912, ii, 1204.

13. Ten Broeck: Boston Med. and Surg. Jour., 1915, clxxiii, 284.

14. Trumpp: Jahrb. f. Kinderh., 1897, xliv, 268.

15. Morse and Crothers: Arch. Pediat., 1909, xxvi, 561.

16. Knox and Meakins: Arch. Int. Med., 1908, ii, 241.

17. Kowitz: München. med. Wchnschr., 1914, lxi, 1341.

18. Williams, E.: Lancet, London, 1912, ii, 511.

men of pyelitis has been emphasized by many writers[19] and is well known to all who have had experience with the disease. MacGowan[20] says he has seen a direct rise and fall of the bacilli in the urine with the neglect or care of the bowels.

Undoubtedly, there are sources of infection other than the gastro-intestinal tract, such as the teeth, tonsils and local septic lesions. Several writers[21] have emphasized this and the necessity of finding and removing the source of infection. The extra-intestinal sources are especially important in those cases in which the organism is some other than the colon bacillus. A patient of mine well illustrates this point: An infant 2 days old had a high temperature, a few impetiginous pustules on the neck and a pyelitis. The organism in the pustules was *Staphylococcus aureus* and the same organism was in the urine. After the healing of the skin lesions the pyelitis quickly disappeared.

The work of Kraus[22] has shown definitely that bacteria may pass through the kidney without causing lesions in its substance. If staphylococci are injected into the ear of a rabbit, they cause lesions in the heart, abdominal wall and pyramids of the kidney passing through the glomeruli without setting up inflammation. Honeij[23] found leprosy bacilli in the urine of patients during the febrile stage of the disease. Brown,[24] Rist and Kindberg[25] and Foulerton and Hillier[26] found tubercle bacilli in the urine of patients whose kidneys were not damaged. Crabtree has injected the paratyphoid organism into the rabbit and recovered it from the urine. At necropsy the kidneys were normal.

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19. Among these may be cited the following:
Pardoe: Brit. Med. Jour., 1910, ii, 1129.
Briscoe: Lancet, London, 1909, ii, 1269.
Hutchinson: Clin. Jour., 1911, xxxviii, 209.
Thompson, W. H.: Med. Rec., New York, 1910, lvii, 907.
Pringle: Practitioner, London, 1911, lxxxvii, 35.
Jeffreys: Quart. Jour. Med., 1911, iv, 267.

20. MacGowan: Jour. Am. Med. Assn., 1915, lxiv, 226.

21. Rawles: Med. Rec., New York, 1911, lxxx, 707; Ibid., 1912, lxxxi, 359. Smith, F. H.: Old Dominion Jour. Med. and Surg., 1914, xix, 77. Nice: South. Med. Jour., 1915, viii, 1027. Grulee and Gaarde: Jour. Am. Med. Assn., 1915, lxv, 312. Huet: Nederl. Tijdschr. v. Geneesk., 1916, p. 521, abstr. Jour. Am. Med. Assn., 1916, lxvi, 993.

22. Kraus: Arch. f. exper. Path. u. Pharmakol., 1896, xxxvii, 1.

23. Honeij: Jour. Infect. Dis., 1915, xvii, 376.

24. Brown, L.: Jour. Am. Med. Assn., 1915, lxiv, 886.

25. Rist and Kindberg: Presse med., 1914, xxii, 177.

26. Foulerton and Hillier: Brit. Med. Jour., 1901, i, 774.

The infection of the pelvis of the kidney from within, that is, by bacteria brought to it by the blood and excreted, seems established.

The possibility of the infection of the kidney substance from infection in the pelvis was shown by Kumita,[27] who demonstrated the extensive lymphatic connection between all parts of the kidney. That such infection actually occurs has been demonstrated by Hugh Cabot and Crabtree[28] and supported by A. Müller.[29]

This statement of the mode of infection in pyelitis satisfies all the conditions except in offering an explanation for the greater frequency of the disease in females. This explanation is not hard to find, for no mention has been made of a very important source of lymphatic and blood infection of the kidney, namely, the pelvic organs. Poirier[30] and Sobotta[31] have shown that the lymphatic vessels draining the pelvic organs are connected by free anastomosis with the kidney. These vessels drain through the thoracic duct into the blood. Sweet and Stewart[32] proved experimentally that when the ureters were cut and sewed into the intestinal canal, if infection of the kidneys occurred, it was through the lymphatics about the ureters not through the lumen of the ureter. Sakata,[33] Sugimura,[34] Bauereisen,[3] J. Thomson,[35] W. B. Clarke,[36] and Eisendrath and Kahn,[37] working on the problem of kidney infection, all come to the same conclusion, that the lymphatics, not the ureters, play the major rôle in conveying direct infection from the pelvic organs to the kidney. If bacteria get into the lymphatics, they may get into the blood through the thoracic duct and thus to the kidney, or possibly into the blood from the infection in the kidney, and cause a pyelitis. Thiele found bacteria in the blood and urine from pelvic infection. Cases of pyelitis following circumcision have been

27. Kumita: Arch. f. Anat. u. Path., Anat. Abt., 1900, xlix, 94.
28. Cabot, H., and Crabtree: Unpublished communication.
29. Müller: Ztschr. f. Urol., 1912, Supplement.
30. Poirier: The Lymphatics, Constable, London, 1903, Translation by Leof.
31. Sobotta: Human Anatomy, 1907.
32. Sweet and Stewart: Surg., Gynec. and Obstet., 1914, xviii, 460. Stewart: Univ. Penn. Med. Bull., 1910, xxiii, 233.
33. Sakata: Arch. f. Anat. u. Physiol., Anat. Abt., 1903, 1.
34. Sugimura: Virchows Arch. f. path. Anat., 1911, xx, 206.
35. Thomson, J.: Quart. Jour. Med., 1909-1910, iii, 251.
36. Clarke, W. B.: Clin. Jour., 1911, xxxviii, 177. Walker: Lancet, London, 1913, i, 435.
37. Eisendrath and Kahn: Jour. Am. Med. Assn., 1916, lxvi, 561.

TABLE 1.—Detailed Record of the Cultures Made from the Secretions of the Vagina in Girls of Various Ages

Case	Age	No Growth	Staphylococci	Streptococci	Gram-Negative Bacilli	Colon	Other Organisms
1	2 hours.....	+					
	30 hours.....	..	+	..	+		
2	6 hours.....	+					
	34 hours.....	..	+				
3*	6 hours.....	..	..	+			
	6 hours.....	..	..	+			
	13 days.....	..	+	+	+		
4	22 hours.....	..	..	+			
5	7½ hours.....	+					
	8 days.....	..	+	+			
6	2 days.....	..	+				
	11 days.....	..	+	+	+		
7	3 days.....	..	+	..	..	..	Spore bearing gram. neg. bac.
8	4 days.....	..	+	..	+		
	9* days.....	..	+	..	+		
9	2½ hours..... ..	+					
	2 days.....	..	+	..	+		
	5 days.....	..	+				
	8 days.....	..	..	+			
10	7 hours.....	+					
	3 days.....	..	+	+	..	..	Gram positive bac.
	6 days.....	..	+				
11	8 days.....	..	+				
12	2 days.....	..	+				
	5 days.....	..	+	..	+		
	8 days.....	..	+	..	..	+	
13	18 hours.....	..	+	+			
	4 days.....	..	+	+			
14	7 hours.....	+					
	3 days.....	..	..	+			
15	2 days.....	..	+	..	+		
	5 days.....	..	+				
16	24 hours.....	+					
17	3 years.....	..	..	+			
	3 years.....	..	..	+			
	3 years.....	..	..	+			
	3 years.....	..	..	..	+		

* Secretion taken from the vulva. † Secretion taken from the urethra.

TABLE 1.—Detailed Record of the Cultures Made from the Secretions of the Vagina in Girls of Various Ages—(*Continued*)

Case	Age	No Growth	Staphylococci	Streptococci	Gram-Negative Bacilli	Colon	Other Organisms
18	8 months.....	..	..	+	+		
	8 months.....	..	+	..	..	+	
19	6 years.....	..	..	..	..	..	Gram negative diplococcus
	6 years.....	..	..	+			
	6 years.....	..	..	+	..	..	Gram negative diplococcus
†	6 years.....	..	..	..	..	..	Gram negative diplococcus
20	2 years.....	..	..	+	+		
	2 years.....	..	..	+	+		
21	8 years.....	..	+				
22	8 years.....	..	..	+			
23	2 months.....	..	..	..	..	+	
24	6 months.....	..	+	+	..	+	
	6 months.....	..	..	..	..	+	
	6 months.....	..	..	..	..	+	
25	5 years.....	..	..	..	+		
26	16 months.....	..	..	..	..	+	
27	3 months.....	..	..	..	..	..	Bacillus fluorescens?
28	4 months.....	..	..	..	..	..	Bacillus fluorescens?
29	3 weeks.....	..	..	+			
30	1 week.....	..	+	+			
31	6 days.....	+					
32	6 days.....	..	+	+			
33	5 days.....	..	..	..	..	+	
34	5 years.....	..	..	..	..	+	
*	5 years.....	..	..	..	..	+	
35	2 years.....	..	..	..	..	+	
†	2 years.....	..	..	+			
36	11 months.....	..	+	+			
†	5 years.....	..	+	+			
37	8 months.....	..	+	+			
	5 years.....	..	..	+			
38	7 months.....	..	..	.	..	+	
39	4 months.....	..	..	..	..	+	
40	3 weeks.....	..	..	..	+		
	Total.....	8	29	29	14	13	

* Secretion taken from the vulva. † Secretion taken from the urethra.

reported by many writers. Rovsing[38] in 1897 reported several cases of pyelitis in young married women, following rupture of the hymen. The female genital organs, with the close proximity of the urethra, vulva and vagina to the rectum and the semi-closed character of the parts, offer every advantage for the entrance and growth of colon bacilli and other bacteria.

To see whether this region was in fact a possible source of infection, I have made seventy-one cultures from the vagina, vulva or urethra of forty infants and young children. One infant 6 hours old and all over 18 hours old, except one infant 6 days old, showed a growth from vaginal culture. All the vulval and urethral cultures were positive. The first organisms to appear were streptococci and staphylococci and then small bacilli—not colon. Colon bacilli were found in vaginal cultures of infants as early as the fifth day.

The colon bacillus was identified by the following characteristics: motile bacillus, gram negative, obtained from characteristic (shiny, dirty, brown, confluent) colony on agar, giving acid coagulation of litmus milk, forming gas in glucose, and producing characteristic (as above) growth on potato.

The other bacillus frequently found was delicate, nonmotile, gram negative, causing no change in litmus milk, forming no gas in glucose and easily outgrown even by streptococci.

These findings are in accord with Schmidgall,[39] who found the vagina of newborns sterile ten out of thirteen times, and by the second day a profuse growth of cocci. The colon bacillus was isolated twelve times out of twenty-one in newborns after the second day. She showed also that the vaginal secretions did not kill off the pathogenic organisms. Others[40] have found bacilli and cocci in the vagina and vulva of infants in differing proportions. Alsberg[41] in adults found the colon bacillus in 100 per cent. of cases in the urethra of women and concludes that it is a regular habitant of the female urethra.

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38. Rovsing: Ann. d. mal. d. org. génito-urin., 1897, xv, 897, 1009, 1121, 1251; Ibid., 1898, xvi, 179, 278.

39. Schmidgall: Beitr. z. Geburtsh u. Gynäk., 1914, xix, 190.

40. Among these may be cited the following:
Menge: Deutsch. med. Wchnschr., 1894, xx, 867.
Strognoff: Monatschr. f. Geburtsh u. Gynäk., 1895, ii, 365.
Vahle: Ztschr. f. Geburtsh u. Gynäk., 1895, xxxii, 368.
Knapp: Monatsch. f. Geburtsh u. Gynäk., 1897, v, 84.
Neujean: Beitr. z. Geburtsh u. Gynäk., 1906, x, 408.

41. Alsberg: Arch. f. Gynäk., 1910, xc, 255.

A possible source of infection with colon bacilli or other bacteria is certainly present in the female vulva, urethra and vagina, and a slight trauma might easily accomplish the entrance of organisms into the lymphatic vessels and blood and thus permit their transportation to the kidney.

I think that we have sufficient evidence to believe that pyelitis is always a blood infection and that the bacteria frequently gain entrance to the blood by the lymphatics. In the uncomplicated cases the lesion remains localized in the pelvis of the kidney, where the organisms are excreted. Secondary infection of the kidney substance may occur by lymphatic channels from the pelvis. Quite possibly these secondary infections account for many "relapses." The source of the infection in the majority of cases, considering males and females together, is the gastro-intestinal tract. Some cases may arise from infection in the skin, teeth or tonsils or in some local septic process. Many cases in females, accounting for the greater number in this sex as compared with the males, arise from bacteria entering the blood, often via the lymphatics, from the urethra, vulva or vagina,

I wish to express my thanks to Dr. Franklin S. Newell for his kindness in permitting me to make cultures from infants at the Boston Lying-In Hospital, and to Dr. Richard S. Eustis and Dr. John W. Hammond, Jr., for assistance in the laboratory.

329 Beacon Street.

DISCUSSION

DR. RACHFORD: Why is this infection more common in females than in males?

DR. HELMHOLZ: There is just one point that I should like to bring out. In some experiments in which Dr. Kretchmer attempted to determine whether in children there was any reflux of injections from the bladder into the ureter, he found that in three out of twelve cases he was able to show, by means of Roentgen pictures taken immediately after the injection, that there was a reflux from the bladder into the ureter.

DR. SMITH: To answer the question of Dr. Rachford, why this infection is more common in females, I would say that I believe it is due to the anatomy of the female parts.

INFANTILE SCURVY

III. ITS INFLUENCE ON GROWTH (LENGTH AND WEIGHT)*

ALFRED F. HESS, M.D.
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In two previous papers[1] on this subject it was shown that pasteurized milk, that is, milk heated to 145 F. for thirty minutes, gradually induces infantile scurvy, unless antiscorbutic diet is given in addition. The fact that this disorder quickly yielded to the substitution of raw for pasteurized milk, or to the addition to the diet of an ounce of orange juice, or the juice of orange peel, was regarded as satisfactory evidence of the true scorbutic nature of the disturbance. The type of malnutrition which gradually develops from a diet of pasteurized milk may be termed subacute scurvy, as it takes some months to develop and, as a rule, does not manifest the pronounced symptoms characteristic of the classic case. In some instances, however, we encounter subperiosteal hemorrhages and the hemorrhagic gums typical of this disorder. That infantile scurvy is not met with more commonly, in view of the widespread use of pasteurized milk as a food for infants, may be ascribed to the fact that orange juice or other antiscorbutic food is so generally given in addition to milk. In other words, although pasteurized milk is to be recommended on account of the safety which it affords, it must be regarded as an incomplete food for infants. That the disease developing under these conditions is subacute in nature is to be attributed to the fact that the "vitimins," which are not overabundant in commercial milk, are not entirely destroyed by pasteurization, so that the infant receives day by day a small amount of these essential substances.

It will be remembered that these cases of scurvy arose in an institution where the use of orange juice was discontinued, in view of the report of the Commission on Milk Standards to the effect that milk does not suffer a destruction of enzymes or other chemical constituents in the course of pasteurization. In the first paper the nature of the

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* Presented in abstract form before the Society of Experimental Biology and Medicine, Dec. 1, 1915. (Vol. XIII, No. 3, Proceedings.)

1. Hess, A. F., and Fish, M.: Am. Jour. Dis. Child., December, 1914, viii, 386. Hess, A. F.: Jour. Am. Med. Assn., 1915, lxv, 1003.

hemorrhagic condition was studied, the question of involvement of the blood or of the blood vessels. In the subsequent paper the symptoms of infantile scurvy were shown to bear an intimate relationship to those of other deficiency diseases, more particularly beriberi. It was pointed out that scurvy should no longer be regarded clinically as a disorder characterized merely by hemorrhages, nor from a pathologic viewpoint merely as one manifesting changes in the bones, but that signs and symptoms of involvement of the heart (enlargement of the right ventricle and tachycardia) and of the peripheral nerves are also evident, so that a broader aspect is demanded. This paper, the third in the series, which is based mainly on the same cases which formed the groundwork of the previous studies, shows how these infants reacted in their growth to alterations in diet, how they grew on a diet consisting of pasteurized milk, sugar and cereal, when they were at the same time receiving orange juice, when the orange juice was discontinued, and when this juice or the juice of the orange peel was again added to the diet. These infants offered a particularly favorable opportunity for observations of this kind because they entered the institution at an early age and remained there for one or more years, and also because they were most carefully observed, weighed daily and measured on admission and every fortnight subsequently. It was thus possible to chart their growth for more than a year and to compare their progress with that of the other infants in the institution. As far as we are aware, no study of this kind has been attempted in connection with scurvy, although it has long been known that the development of the scorbutic condition is generally accompanied by a cessation of gain in weight. Particular interest would seem to be given this investigation as the subacute type of scurvy must be considered not only the most common form of the disorder, but that which passes most often unrecognized. The opportunity presented itself to probe farther into this question of growth and to determine whether there is not likewise a stunting of the normal increment of the skeleton, an interference with the increase in length. This part of the study was judged to be of greater biologic interest than a mere observation of the effect on weight, as it is well established that infants are particularly tenacious of their impulse to grow in length, and are not readily affected in this respect by nutritional disorders, even such as reach a considerable degree of intensity. As Birk[2] has shown, extreme undernourishment is necessary

2. Birk, W.: Berl. klin. Wchnschr., 1911, No. 27.

to bring about stunting. In animals, Aron[3] demonstrated that lack of nutrition led to a decrease of the fat and of the muscle in the body, but that under such conditions the skeleton continued to grow, and the ash content of the body to increase. If, therefore, this function of the body were affected, we must consider that the metabolism must be profoundly disturbed, and the deficiency of nutritional substances far reaching.

First, as to growth measured by weight, the various charts (Figs. 1 to 4) accompanying this article show the effect in this regard. It will be noted that although the infants continued to gain for a month or two following the discontinuance of orange juice, a decided flattening of the weight curve gradually set in, an almost constant level being maintained for weeks and months. This stationary period persisted until antiscorbutic food was once more added to the diet, when a sudden rise made itself evident. This gradual cessation of gain and sharp reaction may be stated to have been the rule, as there was but one instance in which an infant continued to gain for months in spite of the lack of antiscorbutic food. It will be seen from these charts that there was no permanent retardation of weight; in other words, the growth impulse of the body remained unimpaired and had been merely in an inactive or quiescent state. When orange juice was given once more, the rate of growth was abnormally great. There was supergrowth. Furthermore, after a period of extended observation of six months or more, it has been found that this increased rate of growth is maintained until the infant reaches a weight normal for its age. These charts seem to require but little elucidation. We may add that orange juice and orange peel juice, an infusion of one ounce of orange peel in two ounces of water, were equally efficacious in bringing about a sharp increase in weight, and that these substances apparently did not lose their potency by being boiled.

Two cases should be mentioned especially, as they represent a clinical aspect somewhat different from the others. These infants were under 6 months of age and had never received orange juice. It was possible in these instances to observe for how long a period infants will continue to gain steadily in weight on pasteurized milk before it becomes necessary to add orange juice to their diet, and to judge whether they gradually manifest a lack of gain which can be obviated by giving an antiscorbutic foodstuff. It was found that at about the

3. Aron, H.: Biochemie des Wachstums des Menschen und der hoeheren Tiere, Gustav Fischer, 1913, p. 58.

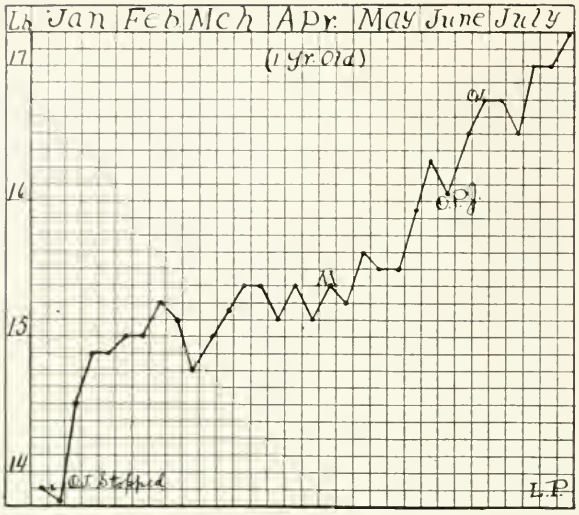

Fig. 1.—Marked gain in weight on orange peel juice and orange juice after lack of gain for three months.

In this and the following figures *O. J.* indicates orange juice; *M.* wheat middlings, and *O. P. J.* orange peel juice.

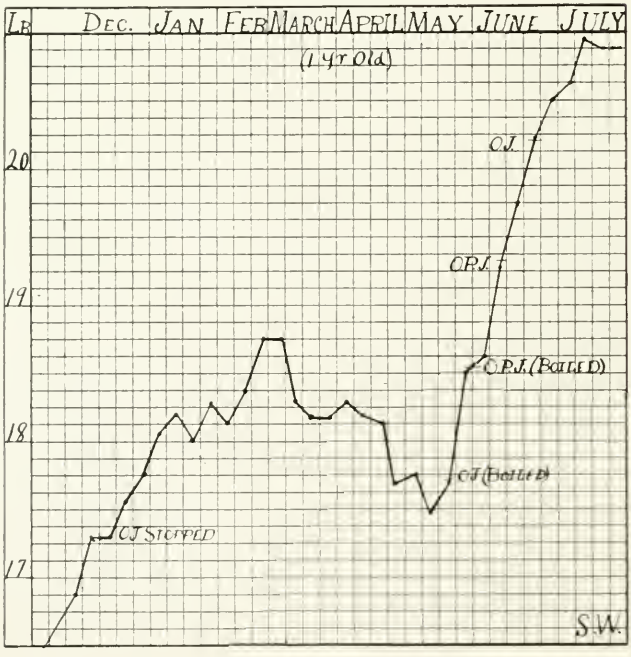

Fig. 2.—Loss of weight checked by boiled orange juice and boiled juice of orange peel.

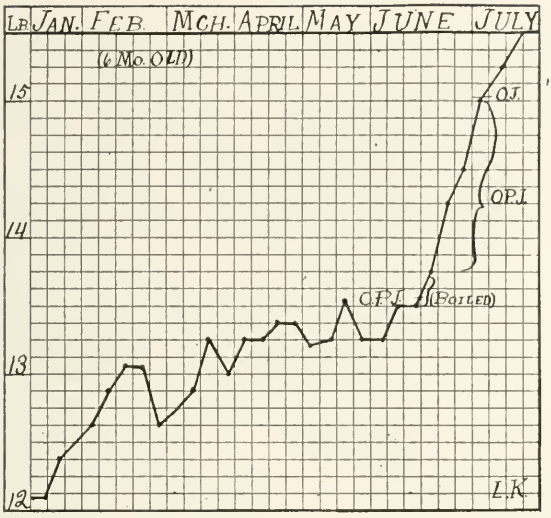

Fig. 3.—Latent scurvy in young infant who had never received orange juice. Scorbutic nature of growth disorder proved by sharp rise in weight on addition of antiscorbutic food to the dietary of pasteurized milk.

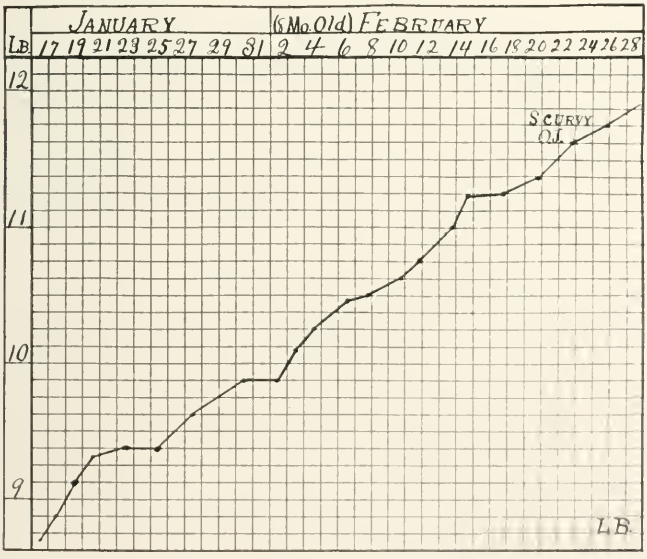

Fig. 4.—Development of scurvy in spite of normal gain in weight in a baby who had been underfed since birth.

seventh or eighth month a gradual but definite falling off was evident, and that this deficiency was at once corrected by adding orange juice. Figure 3 represented this condition very clearly. We note here an infant who gained about one half pound during the months of February, March, April and May, but who in June, when given boiled orange peel juice or orange juice, gained two pounds within a month. There were no other scorbutic signs or symptoms and no loss of appetite during the months of February and March, although the baby was suffering from a progressive form of scurvy. It is probable that this case and a similar one which we encountered are not solitary instances of this kind of reaction, but that many infants fail to gain at this period, the third quarter of the first year of life, for the want of this essential substance in their food, and that unconsciously this deficiency is remedied by adding vegetables and fruit to their dietary. We would therefore urge that antiscorbutics, for instance orange juice, be given infants at an early age. At present, the rule may be said to be to add fruit juices to the dietary at about the sixth month. This period has been chosen as the proper one, probably because scurvy rarely develops during the first half year of life. However, when we reflect that this time incidence is due to the fact that the infant is protected for the first few months of life by the supply of antiscorbutic material which it has received from the mother, and that there must be a constant negative balance of these essential substances dating from the earliest beginning of artificial feeding, it would seem as if a corrective dietary, that is to say, an antiscorbutic food, should be given as soon as practicable. There is no reason that I know of why an infant should not receive orange juice when it is a month old, and, as we have seen, there are strong arguments in favor of such a procedure.

It may be enunciated as a rule, embracing a few exceptions, that the development of the scorbutic state is generally accompanied by a failure to gain in weight. Under certain conditions, however, the weight may follow a perfectly normal course during the entire period. This observation has, from time to time, been made by others, but has received no particular consideration. It may be well therefore to cite in some detail a case of this kind, and discuss one cause of this apparently paradoxical course of events. Figure 4 illustrates this clinical paradox. The baby to whom it refers was admitted to the institution in January and was stated to be only four months of age. As a matter of fact, as we learned later, he was seven and a half months old.

Toward the end of February, when he had been in the institution two months, and in spite of constant and normal gain in weight, to our surprise he manifested unmistakable signs of scurvy—peridental hemorrhage over the upper incisor teeth, which were erupting, and tenderness of the lower ends of the femora. The scorbutic nature of these signs were substantiated by their prompt subsidence on the administration of orange juice.

How is this phenomenon to be explained, normal growth during the development of scurvy, one of the classical nutritional disorders of infancy? The solution is to be found in a careful consideration of the previous diet of the baby. On investigation we found that it was born on June 5, 1915, at term, weighing six pounds, but was never nursed. For the first two weeks it received an indefinite formula prepared by the mother. From June 21 to August 19, that is, for a period of about two months, it was given a formula composed of one-fourth milk, three-fourths water, and 1.5 per cent. sugar, two ounces every three hours. In other words, it was greatly underfed for these two months. In August it weighed 8 pounds, 5 ounces. From August 19 to 27 the formula was 30 ounces water, 12 ounces milk, and about 1 per cent. sugar, four ounces being fed every three hours. This resulted in loss of weight, the baby weighing 7 pounds 15 ounces. On September 7 the formula was made one-half milk, one-half water and 1 per cent. sugar, four ounces every three hours. The underfeeding continued. On December 5 it was transferred to a hospital, where it was given a malt soup preparation for one month. It developed gastro-enteritis on January 17. As the chart shows, the child was admitted to the Hebrew Infant Asylum, weighing about 8¾ pounds at the age of 7½ months.

If we consider the feeding of this infant, we realize that it had been almost continuously undernourished, receiving an insufficient amount of fats and carbohydrates at almost all times. At the asylum the baby was put on Schloss milk, a food containing about 4 per cent. fat and about 6 or 7 per cent. carbohydrates, seven feedings of 4 ounces in the twenty-four hours. On this it remained and, as will be seen, made steady gains until it developed scurvy toward the end of February.

This baby must be regarded as having been partially starved throughout the period following birth, with the result that on receiving a diet rich in fats and carbohydrates, foodstuffs which bring about a marked increase in weight, the reaction of the tissues was necessarily prompt

and prolonged. It explains this type of case, showing that if an infant has received insufficient food, we can compel growth simply by increasing the caloric value of the dietary, notwithstanding the fact that scurvy is developing day by day. It also brings out the salient fact that more than a single cause exists leading to a repression of growth, and that therefore lack of growth must be differentiated if it is to form the basis of study. A deficiency of scurvy vitamins is one cause, lack of sufficient or adequate food is another, and, no doubt, there are still other inciting factors. Whether or not growth occurs, and to what extent, depends on the resultant stimulation which can be brought about by these various impulses. In this instance the primary growth impulse which follows a diet containing a sufficient number of calories had been held in abeyance for so many months through starvation, that when it was once more stimulated to full activity by a liberal diet, it was able to overcome the growth repression which ordinarily accompanies the development of the scorbutic condition.[4]

The foregoing illustration must make it clear that growth does not play an essential or elemental part in the constitution of infantile scurvy. It must likewise render it evident that this study cannot be regarded as concerned with growth in general, but only with the effect of infantile scurvy on growth, as various disorders may affect this function. That such is the case is well known to clinicians and has been shown admirably in relation to animals in the recent investigations of Osborne and Mendel, of McCollum and others, which showed that growth was retarded or stimulated at will by means of diet. The results of these workers cannot, however, be considered as having any bearing on scurvy, for scurvy and growth stunting are by no means identical, either in animals or in infants. It would seem that these remarks are timely in view of a recently published study by McCollum and Davis,[5] in which they show that the growth factor in milk is closely linked to its casein content, and preface their report by drawing an analogy to infantile scurvy, although apparently none of the animals showed any signs of a scorbutic condition.

4. This phenomenon probably also holds good for scurvy in the adult. A scorbutic condition may result from a lack of fresh food; but if the person has been markedly underfed, there may be a gain in weight coincident with the development of the scorbutic condition, provided liberal diet is given, including plenty of carbohydrate and fat.

5. McCollum, E. V., and Davis, M.: Jour. Biol. Chem., November, 1915, p. 247.

Looking at this question from the reverse point of view, one sees clearly that factors which stimulate growth are not necessarily antiscorbutic. For example, McCollum and Davis[6] showed that butter fat, even after it had been heated to a high degree, was able to induce growth, and Osborne and Mendel[7] showed that this fat can be subjected to steam and not lose its growth-producing power. It is nevertheless evident that butter fat in pasteurized milk does not possess sufficient antiscorbutic properties to prevent the development of scurvy, and that substances such as lysin and tryptophan, which possess marked growth-promoting power, and which were present in considerable amount in our diet, were unable to make up for the dietary deficiency and bring about growth. Furthermore, cod liver oil has been found to possess growth-promoting qualities of a high degree, but there is no question that this substance, as has been shown elsewhere,[1] is incapable of preventing the development or accomplish the cure of scurvy. Before reporting additional observations as to the influence of scurvy on growth, let me add that all of the infants under consideration obtained plenty of milk, and all the older ones received cereal in addition. Particular attention was given to their obtaining a sufficient quantity, so that the factor of an insufficient diet might not enter into the question. To this end, when orange juice was discontinued, more cereal was given or the strength of the milk mixture was increased in many instances. In those cases in which there was loss of appetite, particular effort was made to have the infants take the full quantity of food, and, although the total amount consumed in many cases was not quite as much as when they were well, it nevertheless equaled that which many infants in the institution consume and on which they continue to grow.

There is no doubt that considerable of the supergrowth which so clearly follows the giving of orange juice or its equivalent is due to an increased consumption of food. However, it would be a mistake to consider that such is entirely the case. We have reproduced two charts to illustrate this point. The first (Fig. 5) is a daily weight chart of an infant with mild scurvy, and shows the period preceding as well as that following the giving of orange juice, together with the food intake (Schloss milk). Although it will be seen that there was no change in

6. McCollum, E. V., and Davis, M.: Jour. Biol. Chem., 1913, xv, 167.
7. Osborne, T. B., and Mendel, L. F.: Jour. Biol. Chem., May, 1915, p. 381.

the amount of milk taken before and after giving orange juice, there was a marked difference in the gain; the infant increased only 5 ounces in weight during the three weeks in which it did not obtain orange juice, and 12 ounces in ten days following its addition to the diet. Figure 6 shows another aspect of this question. It demonstrates that

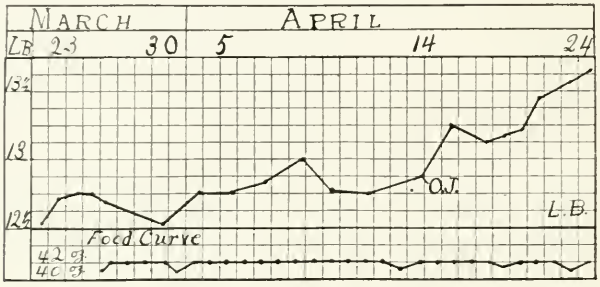

Fig. 5.—Same case as preceding. Detailed chart showing marked gain following the addition of an antiscorbutic to the diet, although amount of food remained the same.

Gain of 5 ounces in three weeks before, and 12 ounces in ten days after orange juice was given.

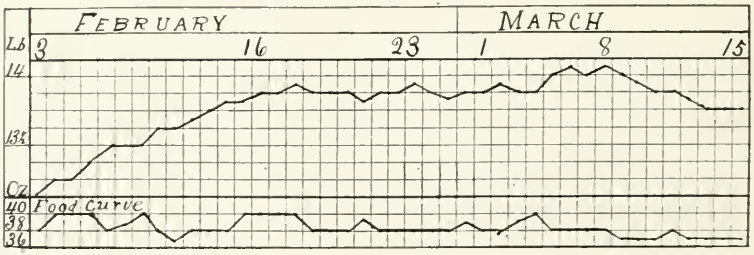

Fig. 6.—Section of a weight chart showing daily weighings during the period when gain still continued and when stationary plane was reached.

Note that the same amount of food was taken daily during the first two weeks of February, when the infant gained 12 ounces, as from the middle of February to the middle of March, when there was no gain whatever.

This baby had latent scurvy and responded promptly to orange juice.

the period of gradual growth stagnation, on which infants fed entirely on pasteurized milk enter as the result of not receiving an antiscorbutic, is not due to a lack of food. Here we note the gradual inception of this stationary phase, from a period of gain, in spite of the fact that the intake of food remained undiminished. It is evident, therefore, that

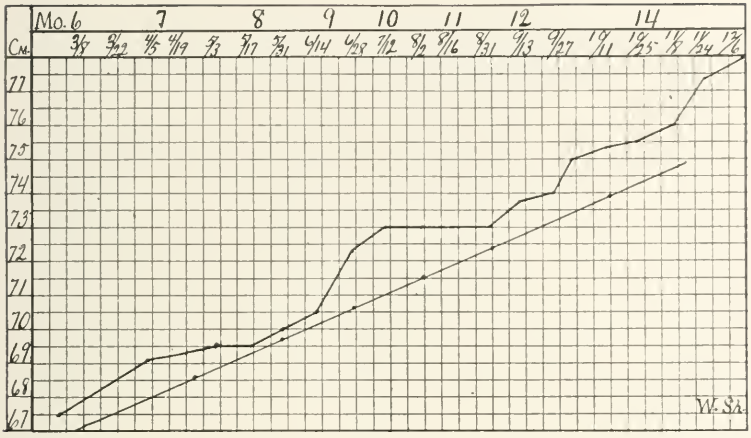

Fig. 7.—Growth in length from the sixth to the fifteenth month of healthy baby receiving orange juice. The lower line represents the average growth.

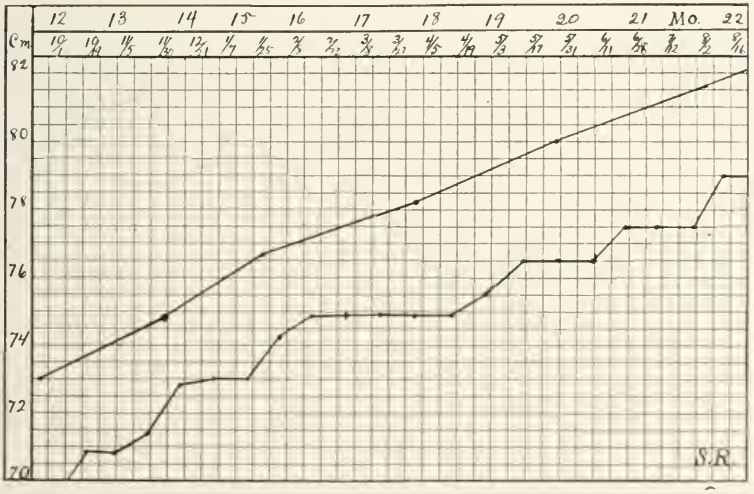

Fig. 8.—Growth in length from the twelfth to the twenty-second month of a very small, healthy baby receiving orange juice.

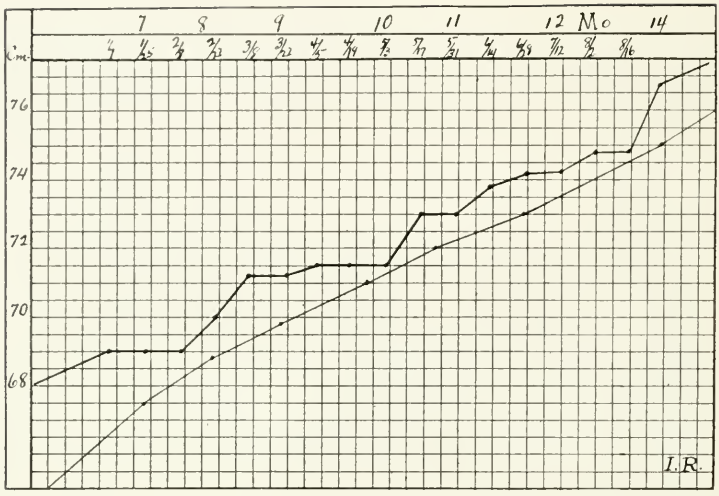

Fig. 9.—Growth in length from the seventh to the fourteenth month of a large healthy baby receiving orange juice.

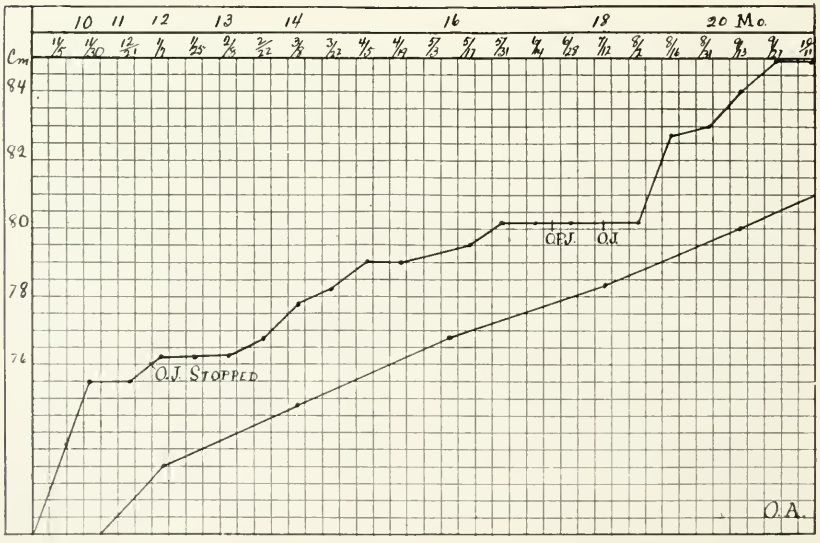

Fig. 10.—Growth in length for a period of five months during which no orange juice was given, compared with subsequent months when it was again added to the diet.

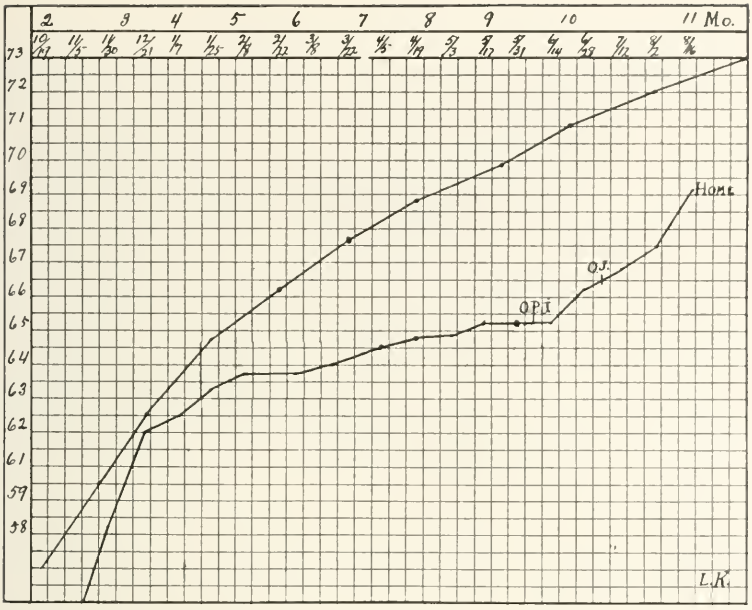

Fig. 11.—Length chart of young infant (illustrated in Fig. 3) who had never received orange juice. Marked reaction in growth in length when an anti-scorbutic was added to the diet.

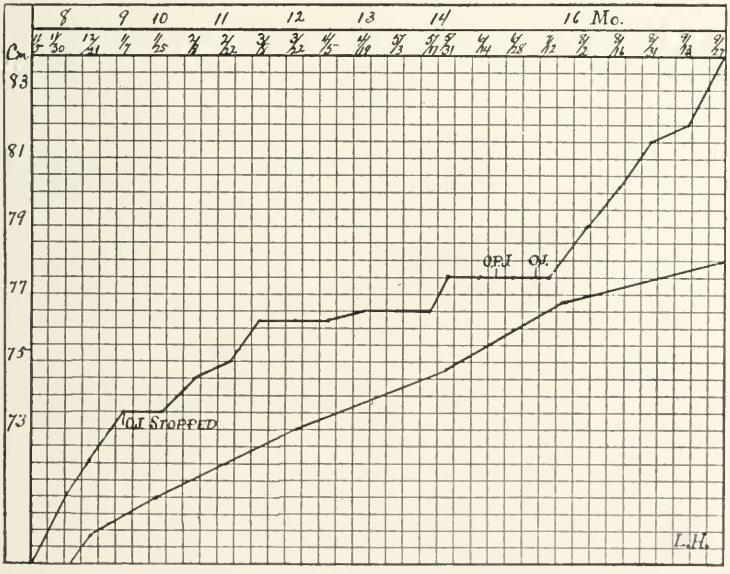

Fig. 12.—Showing retardation of growth in length during the period when no orange juice was given, and supergrowth when it was given once more.

neither the lack of gain in the course of the development of infantile scurvy, nor the increase of weight coincident with its cure, can be considered to be dependent on the caloric value of the dietary.

As has been mentioned above, a study of the growth in length was also carried out, the measurements being taken fortnightly for over a year. In order to furnish a basis for comparison, the growth of ten normal infants who received orange juice, but otherwise the same diet, was followed at the same time. The charts which we reproduce clearly bring out the distinction between the two groups of cases. Figures 7, 8 and 9 illustrate the growth of the normal infants, and constitute a standard by which to judge the others. They portray a consistent, although slightly irregular, growth month by month. Quite in contrast to these curves are those depicted in Figures 10, 11 and 12, representing three infants who did not receive orange juice from January to May.

Figure 11, which represents growth in length complements Figure 3, representing growth in weight, and illustrates the case of a young baby who had never received orange juice, and developed a latent or rudimentary form of scurvy when about eight months of age. These three cases, when contrasted with the normals, leave no question that the scorbutic condition has a decided effect on growth in length as well as in weight, and that this impulse remains unimpaired in both respects and capable of quick response when the essential foodstuff is furnished.

CONCLUSIONS

Although pasteurized milk is to be recommended on account of the security which it affords against infection, we should realize that it is an incomplete food. Unless an antiscorbutic, such as orange juice, the juice of orange peel, or potato water is added, infants will develop scurvy on this diet. This form of scurvy takes some months to develop and may be termed subacute. It must be considered not only the most common form of this disorder, but the one which passes most often unrecognized. In order to guard against it, infants fed exclusively on a diet of pasteurized milk should be given antiscorbutics far earlier than is at present the custom, even as early as at the end of the first month of life.

In the course of the development of infantile scurvy, growth, both in weight and in length, is markedly affected. Under these conditions, weight ceases to increase, and a stationary plane is maintained for weeks or for months. There is a quick response, however, on the

administration of orange juice or its equivalent, indeed supergrowth is thereupon frequently manifested. If, however, an infant has been underfed, an increase in weight may continue throughout the development of the scorbutic condition. Cessation of growth, as well as marked increase in growth, may manifest themselves, although the caloric value of the food remains unchanged, depending merely on the withholding or the addition of essential foodstuffs to the diet.

Measurements showed that growth in length is also retarded during the protracted development of infantile scurvy. This is of greater biologic interest, as simple malnutrition usually does not affect this function in the infant. In this particular supergrowth also follows the addition of the essential foodstuff, showing that the growth impulse has remained uninjured and has been merely held in abeyance.

16 West Eighty-Sixth Street.

DISCUSSION

DR. HOLT: I think that Dr. Hess has established the point that has been under discussion from time to time, whether pasteurized milk can be held responsible for the development of scurvy. It has been my conviction for several years that such was the case, and a number of instances have come under my observation during the last year which have confirmed me in my earlier view. While we all admit the great benefits which have been secured by the introduction of pasteurized milk, in making safe milk about the production and handling of which we were in doubt, the disadvantages of pasteurization have sometimes been denied and sometimes ignored, and, on the part of the dealers supplying pasteurized milk, disputed. Unless we who are interested in the production of clean, raw milk and certified milk make strong our disapproval of the general pasteurization of milk, I fear that it will not be many years before it may be impossible to secure any but pasteurized milk for infant feeding. In one large city in New England I am credibly informed that the health commissioner is about to issue an order that none but pasteurized milk shall be sold in that city, regardless of the conditions of production or certification. It is doubtless true that certification does not always mean safety, for it has sometimes been done by commissions who were either not qualified or were neglectful of their duty. I believe that to scurvy, as to other diseases, there is an individual predisposition which we cannot ignore; and while comparatively few children on pasteurized milk get scurvy, some certainly do. We are less likely to see bad results from its use among the babies of the poor, because this class give other food to their infants much earlier than is usual among the better class of patients. I have observed, as Dr. Morse pointed out at our Stockbridge meeting, that while formerly nearly all the cases of scurvy were seen after the use of proprietary foods, they are now chiefly seen in those fed on pasteurized or boiled milk. I think that the number of cases of scurvy in the community is increasing, and I am glad that the subject has been brought up before the society. In spite of all that has been written about scurvy the number of cases that are still unrecognized is quite large. During the past season I have had no less than four cases that, although under medical obser-

vation, had not been recognized until there was epiphyseal separation at both knees, both shoulders and both ankles. The profession has been taught that there is no danger in pasteurized milk. It is never safe to use this as the sole diet for long periods unless some antiscorbutic is given to counteract this effect. Orange juice should be begun much earlier than is usually the practice. The daily quantity necessary in these cases is a point of some interest. It has been my lot to see a case of scurvy develop in my wards, in a baby who had been taking 1 ounce of orange juice daily for over a month. The infant was taking boiled milk and a pretty large quantity of carbohydrates, which fact, it seems to me, increases the likelihood of the development of scurvy.

DR. HERRMAN: Dr. Hess stated that when he boiled the orange juice, it retained its antiscorbutic power. Why, then, does simply heating the milk destroy the antiscorbutic elements in it?

DR. ADAMS: If I were to select an epitaph to be placed on my tombstone, it would be, "He opposed the commercial pasteurization of milk." I have fought this, and I am going to continue to fight it as long as I have breath in my body.

What Dr. Holt has said, I hope the society will back up, that is, that commercial pasteurization is dangerous and detrimental to the health of children. No institution should be advised to use commercially pasteurized milk just because some sentimental and erratic individuals in the community band themselves together and decide that all children will be killed with tuberculosis unless the milk is pasteurized when delivered to that institution. With Dr. Hess and Dr. Holt, I have, within the last ten days, had cases in children that had been fed on supposedly the best pasteurized milk delivered in the city of Washington. That dairy is constantly furnishing me with work on antiscorbutic lines, yet it passes as one of the best dairies in the entire country. I cannot understand what Dr. Herrman has asked about, why, if the essential antiscorbutic elements are destroyed in the cooking, they are restored by orange juice. To put the children on raw milk and let the orange juice go will settle the question.

I hope that the matter will be thoroughly discussed, as it is a question that has been avoided in this society for the last few years. I will tell you of an instance in my experience.

I was attending a patient in a certain house, and the father asked the dairyman why he had not sent raw milk, as Dr. Adams had ordered. The dairyman said he had not done so because the milk was not fit to deliver raw. That is the whole secret; it is rotten milk, cooked, that is being foisted on the community. I would as soon buy rotten steak and cook it, in the belief that it would not hurt me, as give a child rotten milk that had been pasteurized, expecting that it would not hurt him. I hope that the members will come out strongly against the commercial pasteurization of milk. I am not opposed to home pasteurization under proper supervision, but I am opposed to commercial pasteurization.

DR. A. D. BLACKADER: I have been much interested by Dr. Hess' reference to what he terms the subacute stage of infantile scurvy. During the past winter I have seen in consultation two infants in whom in my opinion such a condition existed. The symptoms were ill-defined and only from the history did I consider them attributable to a developing scorbutus. Both infants had been fed since the first month of life on patent foods. Both were, when I saw them, about 6 months of age. In neither of them had dentition commenced and growth and weight were defective in both. Their nights were restless and

both showed symptoms of increased nervous excitability. In one I thought I detected a slight tenderness over the distal end of the tibia on pressure. Under the use of orange juice and unpasteurized milk all the symptoms disappeared promptly, and the children began to put on weight. It should be recognized by the profession that the symptoms of infantile scorbutus develop slowly and that there is a stage preceding the development of what may be termed the acute manifestations, characterized by symptoms pointing to defective nutrition, in which the diagnosis can be made only by the previous history.

DR. SHAW: Some years ago I was strongly opposed to pasteurization. At that time I made observations with babies fed on raw and on pasteurized milk, and could find absolutely no difference in the results. My opinion has undergone a decided change since I have been connected with the New York state department of health.

During the past two years eighteen epidemics were traced to the milk supply; 834 cases of communicable disease; thirty-seven deaths resulted, which would have been prevented had the milk been pasteurized.

Personally, I do not think that tuberculosis constitutes the great danger from the use of raw milk, but rather do I believe that there is more likelihood of septic sore throat, diphtheria, scarlet fever and typhoid. It has been very definitely proved that the deaths from diarrheal diseases have been practically cut one half in places where the milk has been pasteurized. I now believe that pasteurization is necessary to safeguard the health of the community.

The warning given by Dr. Hess in his valuable paper should be heeded, for he shows how cases of subacute scurvy resulting from the use of pasteurized milk can be very easily prevented. Orange juice, or an infusion of orange peel, can be given as early as the first month, and in a little book which is sent to every mother in the state by the New York state department of health as soon as her baby's birth is registered, it is recommended that orange juice be given to bottle-fed babies after the first month.

DR. EATON: I want to confirm what Dr. Hess has said about the occurrence of scurvy in the subacute and less acute forms after the use of pasteurized milk. I can recall ten such cases that came under my observation last year. I want to say, further, that commercial pasteurized milk is not at all what we call really pasteurized milk. In my part of the country the dealers advertised "perfectly pasteurized milk," and I sent some one to find out how the pasteurization was done. I learned that it was done over a steam drum at fifteen pounds pressure. That is not pasteurization; it is sterilization. The cases that come to my mind were all cases fed on so-called pasteurized milk. When we have milk that is certified under the supervision of a medical milk commission, and when the handling is properly done, we get better results by sticking to the raw certified milk than by pasteurizing all milk. We have had no milk-borne epidemic that we could trace to the certified milk, but we have had from so-called commercially pasteurized milk. Pittsburgh is a milk distributing center for a good many surrounding towns, and it is from these towns that we get a good many of these obscure cases of scurvy.

DR. HAMILL: This is quite as complicated a problem today as when the society made its investigation many years ago. As I understood Dr. Hess' paper, he was not speaking against the pasteurization of milk. Indeed, he distinctly said that pasteurization is sometimes necessary. I do feel, however, with Dr. Holt, that it is important for us to come to the defense of properly prepared raw milk. There is a strong tendency to enforce the pasteurization

of all grades of milk. I have been a member of the American association of medical milk commissions since its organization, and I feel that this association is in part responsible for the attitude of health officers and sanitarians in respect to certified milk; for the reason that the association from its beginning recognized the establishment of, and accepted into membership, commissions that were absolutely unprepared to certify milk. The conditions obtaining in some of the dairies under the certification of these commissions were a menace to the community instead of a protection, since they created a false sense of security. I think that whatever action this society may take should specify definitely what it understands certification to mean.

I am in favor of the pasteurization of all milk other than certified milk. I believe in the pasteurization of milk because I know that it is much more efficiently done than ever before. In some cities, and I think in the city of Philadelphia, we can say that pasteurization is well done. Of course there are grave dangers from unsatisfactory pasteurization and the improper care of milk after pasteurization, but I do not believe that these dangers compare with those resulting from the use of raw milk. Dr. Shaw has emphasized the frequency with which various epidemic diseases result from the use of raw milk, and a thing so easily controlled as scurvy cannot be classed, from the standpoint of a menace to health, with the epidemics that are milk borne. Even though, as I am not yet prepared to admit, there may be cases of scurvy caused by the use of pasteurized milk, if we can control them as easily as Dr. Hess says we can, we should make no comparison between the dangers of pasteurized and unpasteurized milk.

I should like to ask Dr. Hess on how many cases he has based his opinion regarding pasteurization as a cause of scurvy, and what he recognizes as "the mild manifestations of scurvy." I should also like to know whether he has ever had the experience of seeing cases of the type that he has presented today develop while the child was being fed on raw milk modifications. In my experience I have had as many cases of the type he speaks of from the use of raw milk as when pasteurized milk has been used.

Regarding the statement of Dr. Holt that scurvy is on the increase in New York, I wish to say that I do not believe this to be true in Philadelphia.

DR. COIT: It has been my experience that since the municipal orders for the pasteurization of all milk went into effect in Newark, scurvy has increased. Whether there is a relation between pasteurization per se and scurvy, I am not prepared to say. A few instances prove nothing. Dr. Hess' figures, which are taken from an institution, are more convincing than individual cases, because they allow of the observation of the cases over a long period. I therefore recognize the value of his figures, but I should like to know about the temperature of the air and the rapidity of the circulation of the air in the ward, the antecedents of the babies, their viability before admission and during their treatment in the institution.

I think that the most disquieting thing to us as medical men is the trend toward this universal pasteurization of milk. I do, myself, pasteurize, or refine, the milk. I have discarded the word "pasteurization," because I find that I can accomplish more with the mothers by the use of the word "refine." I tell these women to refine the milk and I can hypnotize them into doing it; but I cannot by using the term pasteurization, which has somehow got on my nerves, as well as on those of everybody else.

The most important point in connection with this problem is that of getting initially clean milk. We should accomplish more with that, if we could always

get it, than with the pasteurization of miscellaneous lots of milk. I am opposed to commercial pasteurization because of the imperfect manner in which the process is carried out and on account of the character of the employees who do it. These people, dragged out of bed at 4 a. m., without sleep enough, will not look after the technic as it should be looked after in order to make the milk safe. I am not opposed to pasteurizing the milk at home under proper supervision. I have pasteurized, or refined, at home, without obtaining scurvy, but I think that it is important for this society to emphasize the value of a raw, clean milk that is certified. We should carry our protest to a point where we can exert an influence on the municipal authorities to prevent their making rules to keep us from getting what we need.

DR. HEIMAN: We should have laws to govern the commercial pasteurization of milk. We still have scurvy and rickets in our midst, whether we give the milk raw or pasteurized. Pasteurized milk will soon cease to be pasteurized, if it is not kept properly after it is opened.

I occasionally gave five drops of orange juice in water with sugar to infants at the age of 1 month. Fruit juices contain the proper salts requisite for the growth of the body, and in giving them we are furnishing the material whose absence would produce not only rickets, but also scurvy. Therefore, I am in favor of their early administration.

DR. VAN INGEN: It seems to me that in discussing the increased occurrence of scurvy since pasteurization of milk became general, more emphasis might be laid on the decreasing death rate from diarrheal disease. The death rate from scurvy has not increased, but that from diarrheal disease has decreased enormously.

DR. LADD: I have seen half a dozen cases of scurvy develop among babies who were presumably fed on raw milk. On investigation I found that an error had been made in overheating the milk before giving it to the babies. There was in each case a definite history of the mother's taking the bottle and putting it in boiling water and leaving it there for a considerable period of time, so that the babies were practically getting boiled or pasteurized milk, although they were supposed to be getting unpasteurized or raw milk.

DR. FREEMAN: I should like to ask Dr. Hess whether he tried giving orange juice to any babies that were not gaining on raw milk.

DR. HESS: I do not feel that the conclusions to be drawn from this paper is that pasteurized milk is not of any advantage. In fact, in my conclusions I prefaced my remarks by saying that it is of advantage. The conclusion to be drawn is rather that pasteurized milk is an incomplete food, that it is inadequate in itself. If this fact is realized and acted on, it will be a boon to pasteurized milk producers, because there will be fewer cases of scurvy following its use and better results obtained. All that is necessary is to give, in connection with it, either orange juice or potato water. You can make potato water instead of barley water. Use one spoonful of mashed potato to a pint of water, and it will be all right. The commercial potato flour has no beneficial effect.

Every one realizes that there is a predisposition to scurvy, whether infantile or adult, in certain individuals. That was realized years ago when there was so much scurvy aboard ships. It is known now, also, that this is true in connection with beriberi. Some persons get beriberi and some do not, although they have been on the same food and in the same places. As regards infantile

scurvy, the susceptibility depends partly on the amount of essential substances that the mother had and the food that she took during her pregnancy, as well as on how long the infants were nursed.

Dr. Herrman asked how it is that boiling the orange juice does not destroy its essential substances, whereas boiling the milk does. That is well known in various substances. A great deal depends on the medium. Certain substances will stand boiling in a watery solution, for instance, orange juice, which will not stand boiling in a medium rich in fats and proteids, such as milk.

In answer to Dr. Hamill, I would say that the symptoms of the scurvy were hemorrhages of the periosteum, petechial hemorrhages, hemorrhages of the gums, hemorrhages into the muscles, enlargement of the heart, tachycardia, and the other symptoms that I detailed in two previous papers. The control cases, of which there were as many as those that had pasteurized milk, obtained orange juice, yet in no instance did any of them develop scurvy. When either orange juice or raw milk was given in the cases with scurvy, there was a sharp reaction in weight and in the clearing up of the symptoms.

As to what is a vitamin, that is difficult to answer. Funk, who devised the term, thought that he had it isolated, but later found that it was not pure. The name is a good one, because it helps to designate the substance essential in scurvy, beriberi, pellagra, etc.

I wish that Dr. Coit would come over to our institution and satisfy himself in regard to the viability of the children there. They are, of course, institutional children, but they look as well as those in their homes. It is a model institution, and has plenty of fresh air. The weight of the children has been taken every day for six months previous to the beginning of the test. It is not as if they just came to the institution as they would to a hospital.

Dr. Freeman asked whether I had tried the effect of orange juice in other cases than those on pasteurized milk. No, not especially in this connection. I could look up the charts and see what happened, but I did not make that particular test.

TRANSIENT ABDOMINAL TUMOR IN A CHILD OF FIVE YEARS WITH REDUNDANT COLON

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AND
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The complaint in this case was the periodic occurrence of abdominal tumor. The patient was the only child of young and healthy parents, though the mother might be said to be of a nervous temperament. The birth weight was 11¾ pounds and the labor was tedious, though a head presentation, delivery being finally effected, after forty-eight hours, by instrumentation. No difficulty was experienced, however, in establishing respiration, and the infant was normally nourished until two days after birth, when a promising lactation for some reason failed. After this the child ran the gauntlet of proprietary foods, including Eskay's, Mellin's and finally Horlick's malted milk, which was continued well into the second year. He sat up at five months, began the eruption of teeth at eight months and walked at nineteen months. With the exception of frequent attacks of rhinitis, to correct which an adenoid operation was performed at the age of 2½ years, the patient escaped all of the diseases peculiar to childhood, progressing in a fairly normal manner to the age of 3½ years.

In December, 1914, approximately a year before my first examination, the patient became suddenly ill in the night, with an attack characterized by extreme nausea and severe vomiting and the appearance of a rounded tumor in the hypogastrium, simulating a distended bladder. The vomiting, to judge from the description, was simply bile-stained gastric juice and at no time stercoraceous. The tumor was elastic, but not especially tender to touch. There was no history of previous disturbance in the regularity of the bowel, as to constipation or diarrhea. Fever was not present.

The physician called at the time had evidently made a diagnosis of intussusception and had completed plans for an immediate removal to the hospital for operation. Returning a few hours later for the patient, he had been, as could be well imagined, much surprised to find that the mass had spontaneously disappeared and the patient recovered.

After this initial appearance these attacks had recurred at varying intervals, seldom less than three weeks and on several occasions as long as six weeks. They had varied in the severity of associated symptoms and likewise in duration, seldom, however, lasting over two days. The tumor had invariably appeared first over the region of the bladder, sometimes larger, sometimes smaller, moved about the abdomen spontaneously and finally disappeared. Its appearance had always been associated with nausea and vomiting, and its disappearance with a pronounced paroxysm of abdominal pain. Following the first attack there had been some tendency to constipation, but the bowels had been kept freely open by the daily employment of mineral oil by mouth. The diet had been well regulated and in the intervals the patient had quickly recovered lost weight. Ordinarily the child was quite normal, played actively and appeared in good health. No prodromal symptoms had been observed.

At the time of my first examination, I found the patient in bed lying on his back, thighs partially flexed. The attack was several hours old and there was still some nausea. Presenting in the hypogastrium was a smooth tumor about the size of an orange, elastic, but not tender to touch, and dull on percussion.

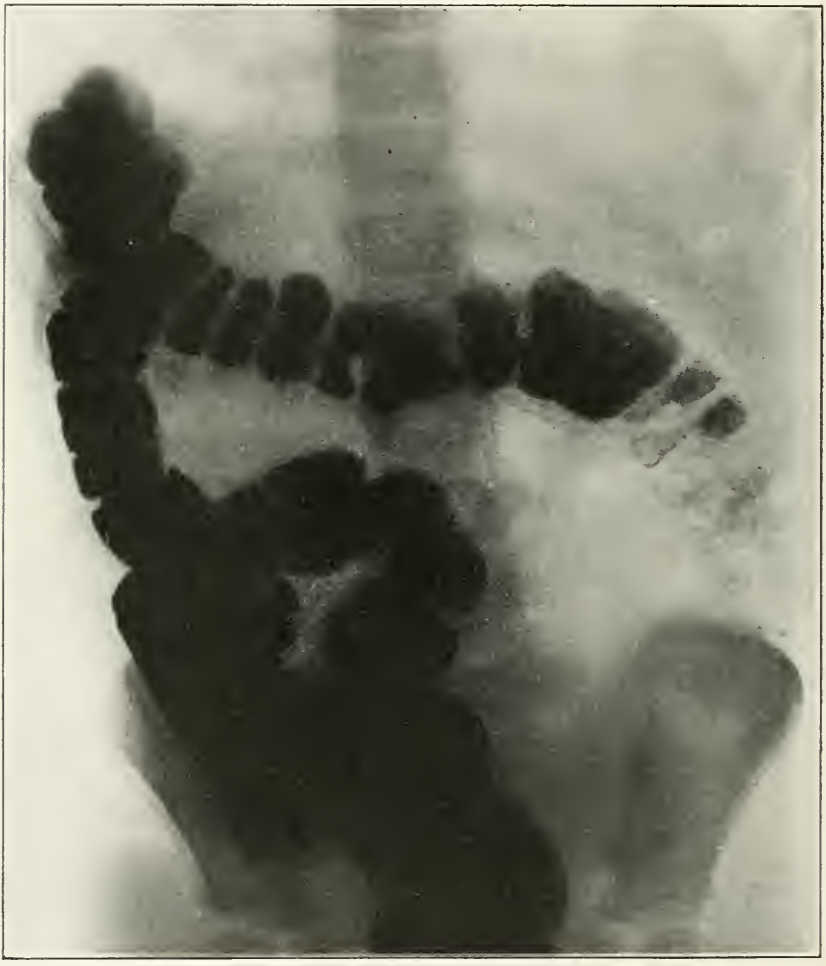

Fig. 1.—Roentgenogram taken tenth minute after bismuth flow commenced.

It was palpable by rectal examination and suggested strongly a distended bladder. The mass was, however, freely movable, it being possible, without undue force, to manipulate it about the entire abdomen. There was a fairly well-pronounced beading of the ribs. The pulse was rapid, but regular. The

temperature normal. A leukocyte count gave 11,500. The von Pirquet and Wassermann tests were negative. No further significant facts were observed.

Under restricted feeding and large enemas slowly administered, the mass spontaneously disappeared. An examination of the abdomen subsequently was absolutely negative.

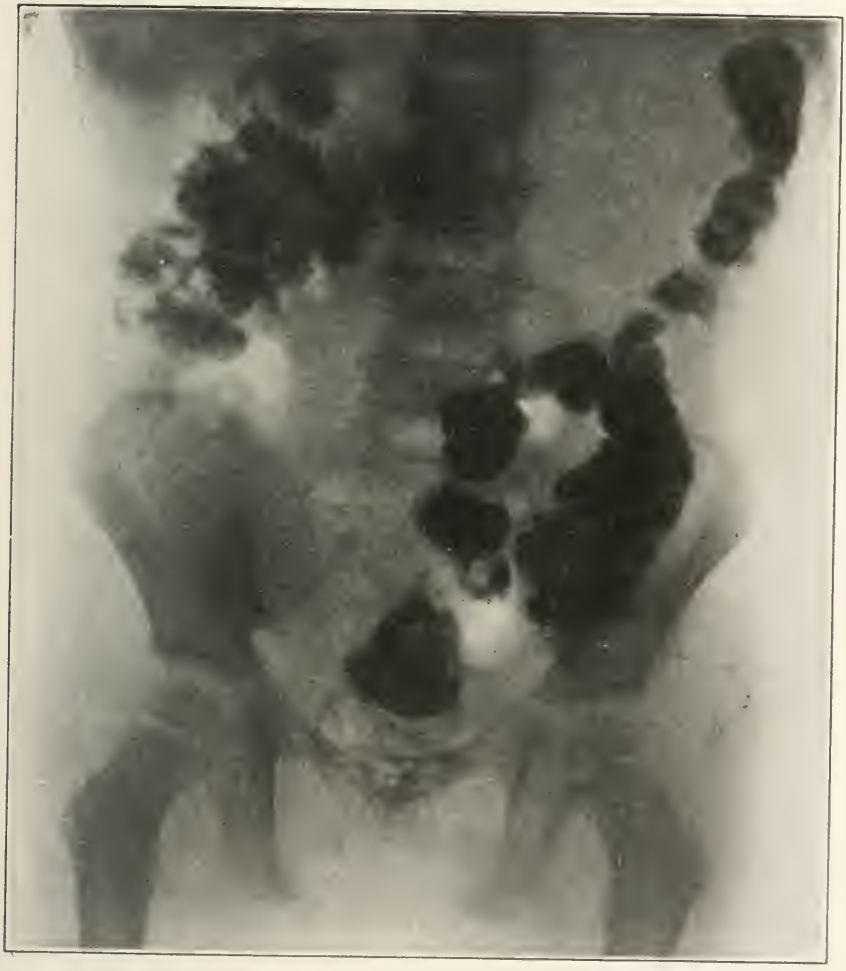

Fig. 2.—Roentgenogram taken at twenty-fourth hour after bismuth enema.

Through the courteous cooperation of Dr. J. H. Selby, a very thorough Roentgen study of the case was made between and during attacks. In this connection I believe that I cannot do better than read Dr. Selby's own report. Examination was made March 5, 1915:

"Findings: Original plates, both back down and face down before the bismuth enema, were negative. Twelve ounces of suspended bismuth subcarbonate were injected by gravity and the visualized filling observed. Plate records were made at the second, fourth, seventh, tenth and thirtieth minute after the flow commenced. The ampulla filled normally, the bismuth column passing vertically, almost in a straight line, to the level of the second lumbar, slightly to the left of the midline, where it turned sharply downward a distance of six inches to the left iliac fossa, at which point it turned sharply on itself passing upward to the diaphragm, when it again turned on itself and descended at a posterior level for three inches before crossing as the transverse colon at the second lumbar. The hepatic flexure is on a level with the transverse colon. The cecum occupies a position one inch above the right iliac crest. The bismuth column reached the cecum in six minutes. *By manipulation the redundant sigmoid or distal portion of the colon can be made to swing over toward the right side and back to the left at will.*

"At the twenty-fourth hour there is considerable bismuth residue in almost the entire colon. The aforesaid redundant colon is distinctly outlined.

"Examination made March 27, 1915:

"Findings: A tumor mass the size of a large orange is palpated in the right upper quadrant. The bismuth injection showed the mass to be redundant descending colon. Visualized palpation reduced the tumor."

CONCLUSIONS

The clinical history, in the light of the Roentgen-ray findings, would seem to justify the assumption that the phantom tumor was the result of a temporary kinking of the redundant colon (or sigmoid), incident to its displacement to the right, which was followed by either fecal or gaseous distention in the loop. When the loop filled itself to a certain point, it swung gradually to the left and automatically unkinked itself, with a disappearance of the tumor mass.

SARCOMA OF THE KIDNEY TREATED BY THE ROENTGEN RAY

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CINCINNATI

It is generally accepted as axiomatic that the only hope in cases of sarcoma of the kidney in childhood lies in early nephrectomy. Even under this procedure the mortality is very high on account of the likelihood of metastases, although the operation itself may be well borne.

The following case is reported because the growth was so large that no surgeon was willing to undertake its removal. For this reason recourse was had to treatment by the Roentgen ray. For a time there was marked improvement. The tumor became much smaller in size, and the child gained in weight and strength. After a time, however, the tumor began to increase in size again. Later, the child contracted measles, with complicating bronchopneumonia. At necropsy the actual results of the Roentgen ray treatment on the tumor mass could be studied. The report herewith submitted is presented because of the opportunity offered to study the effects of intensive Roentgen-ray treatment in a case of this sort.

W. S., boy, white, aged 4 years, was admitted to the pediatric service of the Cincinnati General Hospital on Oct. 20, 1915. The history was one of increasing languor and lassitude, with loss of appetite and anemia. The mother had noticed a mass in the abdomen three months before the child was brought to the hospital. A physician outside had suggested Roentgen-ray treatments. Two of these were given by a roentgenologist. After each of these treatments the boy vomited and passed almost pure blood for a day. This statement by the mother was later confirmed by the roentgenologist himself. For a time after the treatments the boy seemed better, but the improvement did not last.

On examination the child was found to be poorly nourished. Except for the condition of the abdomen, the physical findings were not of moment.

The entire left abdomen was filled by a tumor mass, extending from the costal margin in the nipple line to 3 cm. above the symphysis. The tumor extended 1 cm. to the left of the umbilicus. It was hard, distinctly nodular, apparently not tender to pressure and could be moved forward by pressure from behind.

Uranalysis on admission showed distinct microscopic hematuria. The blood showed a secondary anemia. Fluoroscopic examination with colon partly filled with gas showed a sharply defined dark shadow in the region normally occupied by the kidney. Roentgen-ray plate of the lungs for the characteristic metastatic sarcomatous shadows was negative.

In view of the fact that all of the surgeons who saw the child advised against operation because of the apparent hopelessness of the case, Roentgen-ray treatments were instituted.

Treatments were given with the Coolidge tube. Three areas, front, back and side of the tumor, were covered at each treatment, except the first and second, when one and two areas, respectively, were treated. Twenty treatments were given at intervals of about a week with a dosage as indicated in the table. The distance in all treatments was 8 inches, with a spark gap of 9 inches.

TABLE 1.—DOSAGE EMPLOYED IN ROENTGEN-RAY TREATMENTS

Date	Ma. Seconds
1915—	
Oct. 30	10
Nov 5	15
Nov. 9	15
Nov. 15	20
Nov. 23	25
Dec. 1	25
Dec. 8	25
Dec. 15	25
Dec. 24	25
Dec. 29	25
1916—	
Jan. 4	25
Jan. 12	25
Jan. 19	25
Jan. 26	25
Feb. 5	25
Feb. 12	25
Feb. 21	25
March 3	50
March 10	50
March 17	50

Before each Roentgen-ray treatment the child was given full doses of potassium citrate for a day. As a result of this alkalinization, no Roentgen-ray toxemia followed any of the treatments, except the last. Neither was there any increase of the blood in the urine after the treatments.

After the seventh treatment, given on December 8, it was noted that the tumor had decreased very markedly in size. The child had gained several pounds in weight, looked rosy and well and played like an apparently normal child. In January the child had an attack of influenza, then epidemic in the wards, with double otitis media. The recovery was prompt. By March 1 the child was again very listless and apathetic. The tumor had grown appreciably in size. On March 30 the boy came down with measles, and death occurred on April 4.

The necropsy showed a sarcoma of the left kidney with small metastasis in both lungs and in the liver. The complete pathologic report is not given here.

At my request Prof. P. G. Woolley, pathologist to the hospital, made a microscopic examination of the tumor itself, with reference to

the effects of the Roentgen ray on the growth. His report is herewith submitted:

Specimens for microscopic examination were removed from five different points in the tumor, one from near the upper pole, one from near the lower pole, one from the middle of the tumor at the edge of a hemorrhagic area, and the other two from intermediate portions. The capsule of the tumor was thick and hyaline like that seen in *Zuckergussleber*.

The stained sections showed the most widespread and generally diffuse necrotic changes, with no evidence of inflammatory reaction. Even the stroma showed degenerative changes, associated with irregular areas of edema. The parenchyma was almost completely necrotic, and, except in a few areas, chiefly near the lower pole, showed almost no evidence of structure. One could discern the remains of stroma and parenchyma, by means of the staining reactions, but all the histologic cellular structures were lost. Karyorrhexis and karyolysis were obvious and the general appearances suggested those seen in areas of diffuse caseation. The capsule of the whole tumor mass was, on the other hand, hyaline, and, especially about the blood vessels, showed the structure of hyaline connective tissue. At no place was there any evidence of malignant cellular infiltration.

In the areas where some tumor structure persisted, the appearances were those of an alveolar sarcoma, and in these areas short spindle cells and round cells were present, chiefly the latter. In these areas the capillary vessels were healthy. About the margins of these tumorous foci the tumor cells and the interstitial cells were both changed. The former showed, first, pyknosis, and, as the areas of complete degeneration were approached, rhexis and swelling; the latter, edema and vacuolization.

The fact that the whole necrotic process was so widespread in such a large tumor mass; that there was no evidence of vascular thrombosis in the main vessels and no evidence of infarction; and that the degenerative process appeared to be a gradually progressive one, indicates that the Roentgen-ray treatments were at least partially the cause of the retrogression.

In view of some recently reported cases of hypernephromas of the kidney cured by the Roentgen ray it has seemed worth while to put on record this failure of the treatment in a sarcoma of the kidney in childhood.

Yet it should not be forgotten that the case was a particularly unfavorable one. Unquestionably, when a nephrectomy can be done with any prospect of success, it should be the procedure of choice. But it must be remembered that the mortality under surgical procedure is very high.

In view of the changes effected in the tumor mass by the Roentgen ray in this case (and the fact being admitted that one case does not permit the drawing of any sweeping conclusions), it seems justifiable to say that if nephrectomy is contraindicated in a case of sarcoma of the kidney, the Roentgen ray should be given a thorough trial.

4 West Seventh Street.

REPORT OF A CASE OF INFLUENZA IN AN INFANT

WITH TWO UNUSUAL COMPLICATIONS: PURPURA HEMORRHAGICA AND SUBCUTANEOUS EMPHYSEMA

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On April 7 last I was asked by Dr. S. Moore to see the baby and obtained the following history from him:

The father and mother are both well and healthy, aged 30 and 28, respectively, English. They have two children, one, aged 2½ years and the patient, a boy, aged 6½ months. Both were well and healthy till the father introduced grippe into the house. In due course his wife, the two children, and an uncle became infected.

The baby has nursed exclusively, has always been well and healthy and weighed 15 pounds before the present sickness.

The baby was taken ill with grippe on March 28, last. Dr. Moore did not see him till April 6, when he found dry and moist râles over each side posteriorly and also a well-marked lobar pneumonia at the right base. The temperature was 104, pulse 140, respirations 60. In addition there was a purpuric rash over parts of the body, face (particularly the chin), shoulders, arms, chest, legs and feet. The petechiae varied in size from a mere dot to one patch on the left shoulder the size of a 10-cent piece. Another patch on the left cheek was slightly smaller. These were the only two patches of any size, all the others being about the size of a pinhead, some smaller, a few larger. The two large ones had a punched-out feeling to the palpating finger, as if they had previously contained fluid. The skin, however, was unbroken and there had been no discharge.

Physical examination showed a big well-nourished baby with a lobar pneumonia at the right base and a few râles on either side. There was also a well-marked purpuric or petechial rash, as mentioned above, which the mother stated had been present almost from the appearance of the first symptoms of his illness. His temperature was 102.6, pulse 160, respirations 60. There was a cough, which was neither frequent nor violent.

Apart from the purpura the prognosis seemed fairly good.

On April 13 the attending physician noticed a slight swelling at the sides of the neck, under the chin, and down over the upper part of the chest. At his second visit the same day the swelling had increased. The following day the swelling had markedly increased. In the afternoon of the day (the 16th) I saw the infant a second time the temperature was 98.4, pulse 120, respirations 40; the cough was less frequent and less severe. The lung had about cleared, though many râles were to be heard on the left side. The purpuric

spots had increased in number, especially on the chin, the shoulders and forearms. The large one on the left shoulder was about ½ inch in diameter and elevated. The swelling around the neck, chin, and lower cheeks was so great that the chin was crowded up and the head forced back. It was tense, tympanitic, and crackling under the fingers. It extended from ear to ear and from the lower lip to the level of the third ribs in the midline. It was symmetrical, the sides being enlarged equally, and the lower border on the chest was semicircular in outline. The swelling was obviously emphysematous and had been noticed for a little over twenty-four hours. Though the chin was crowded up and the head forced back, the baby seemed fairly comfortable and looked about him in a contented way, even while I was examining the swelling.

I have not heretofore seen purpura or emphysema as a complication or sequel to influenza, either in my own practice or consultation. The two conditions occurring in the same patient at the same time prompted me to ask a friend if he would take a photograph, which I pass around.

I regret to say that neither the rash nor the swelling show as well as I had hoped. It does not do justice to patient or photographer.

Later on Dr. Moore telephoned me that the emphysema gradually improved and within five days from the date I saw him last it had almost disappeared. On the 19th, he had an extra severe coughing spell, when the emphysema suddenly became more marked than ever. From then on his breathing became embarrassed and he died within twenty-four hours afterward, apparently from edema of the lungs, the emphysema not lessening.

A necropsy was not allowed.

Purpura as a complication of influenza is mentioned only once, as far as I am able to discover from the records of the Academy of Medicine, Toronto. H. P. Hawkins[1] was able to quote seven cases with a rash in 1,000 cases of influenza at St. Thomas Hospital, London. From the description of these cases some were undoubtedly medicinal rashes and were urticarial or erythematous. In one case the rash was produced by 80 grains of sodium salicylate. Concerning his sixth case he states: "The patient had had no medicine and had never suffered from purpura before." This is the only reference to the word purpura in the histories of his seven cases. Therefore one must conclude that purpura as a complication of influenza is infrequent.

The rash in the case I saw I looked on as due to the influenza bacillus, just as one considers the purpuric rash in rheumatism to be due to rheumatic bacillus.

Instances of subcutaneous emphysema are not so uncommon. I have not, however, seen a case complicating either influenza or pneumonia, which latter complication the infant had when the emphysema

1. Hawkins, H. P.: Occurrence of a Rash in Influenza, Lancet, London, January, 1890, i, 191.

occurred. The coughing during either the influenza or the pneumonia was neither frequent, paroxysmal, nor prolonged. An extra severe coughing spell, however, preceded each emphysematous swelling.

Emphysema is mentioned in a few textbooks as occurring occasionally in pertussis, bronchitis, etc., but I have not seen it mentioned in connection with influenza.

A BRIEF REPORT OF SIXTY-EIGHT BLOOD EXAMINATIONS IN INFANCY

WITH A REVIEW OF THE RECENT LITERATURE ON THE BLOOD IN INFANTS

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The work embodied in this paper has occupied a period of several months. Nearly all the infants were residents of the Child Saving Institute. This institute receives children for care and adoption. It is primarily a home, not a hospital. The infant ward contains never less than thirty infants under 6 months. They are being received and discharged constantly. No infant included in this list was in the institute for a less time than one month. None that presented any evidence of syphilis or other infection was included in the list. After doing a certain amount of preliminary work, the writer made a careful search through the current literature to determine what had been done in this line. Before presenting the work done by Drs. Johnson and Moore, we present the following brief abstract. In this work the writers were materially assisted by Miss Ruth Warner, a senior student. We limited our study to current periodicals for the years 1910 to 1915 inclusive, and the following publications were carefully examined for any articles on the blood of infants, for the above period:

Boston Med. and Surg. Jour., Arch. Pediat., Jour. Am. Med. Assn., Am. Jour. Med. Research, Johns Hopkins Hosp. Reports, Am. Jour. Dis. Child., Jour. Infect. Dis., Med. Rec., New York, Lancet, London, Jour. Exper. Med., Pediatrics, Jour. Path. and Bacteriol., Arch. Int. Med., Brit. Med. Jour., Brit. Jour. Dis. Child.

We believe our abstract will be found to comprise all articles concerning the blood in infants. With the exception of one article, all are from American or English literature. In the above journals there were a number of abstracts from both foreign and English literature, which are not included in this review.

Morse[1] counted platelets in twelve normal infants during first nineteen days of life, at least one count being made for each day, and usually more. Counts at birth varied from 100,000 to 412,000. If count was extremely high at birth it decreased in a few days and vice versa, so that all infants after a week showed 350,000 to 450,000. There was no correlation between the weight of the child and the number of platelets. Three babies aged 4, 2, and 11 days respectively, showing idiopathic icterus, showed a marked increase in platelets, which reached a maximum as jaundice cleared away. Two cases of hemorrhagic disease of the new-born were studied. In the first was bleeding from umbilicus, nose and stomach, with hemorrhagic spots on the roof of the mouth and skin; it was treated with rabbit serum; its recovery was accompanied by rapid increase of platelets (from normal count), which reached a maximum on the eleventh day; the erythrocytes and hemoglobin were only slightly reduced; leukocytes were slightly increased. The second had no serum, but recovered with a like increase of platelets, which reached a maximum on the thirteenth day; this case, however, was marked by anemia and the blood regenerated only slowly; the patient also had a slight leukocytosis. A platelet count made on a baby with dermatitis exfoliativa neonatorum the day before its death showed 4,729,000 erythrocytes, 57,000 leukocytes, 279,000 platelets, 80 per cent. hemoglobin. A case of pemphigus foliaceous neonatorum showed 658,000 platelets, 15,000 leukocytes; four days later during improvement, 524,000 platelets, 40,000 leukocytes. He drew these conclusions:

Platelets vary in number at birth exceedingly, but are uniformly numerous and do not vary so much after the first week (from 350,000 to 450,000). Platelets increase in icterus neonatorum; in hemorrhagic diseases of the new-born, there is no diminution at the onset, but a posthemorrhagic increase with a late maximum; in skin lesions of infants count may be higher or lower according to the condition of the child.

Since[2] one of the arguments against the regenerative and in favor of the degenerative nature of basophilic granules in the erythrocytes has been the frequent failure to find them in the blood of new-born infants and in human embryos, Konig has reexamined the field with the

1. Morse: Blood Platelets of New-Born, Boston Med. and Surg. Jour., No. 12, clxvi, 448.

2. Blood of New-Born Infants, Editorial in Am. Jour. Med. Sc., 1910, cxl, 598.

following results; basophilic granules are found both in new-born infants (from 4 to 5 per cent. of cases) and in human embryos (twice in six cases). Neucleated red cells were found in 92 per cent. of new-born babes examined.

S. Cobiliner[3] shows by examination of the blood of a number of infants that nurslings normally have a much greater sugar content in the blood than adults; that in cases of exudative diathesis there is hyperglycemia; that in dyspepsias and intoxications the blood sugar content is not increased; that in cases of decomposition or putrefactive disturbances in the intestines there is hypoglycemia, which gradually reaches the normal as patient improves. In so-called cases of salt fever there may be hyperglycemia.

Cannata[4] obtained constantly negative results in thirty-one healthy babes whose serum was tested for epinephrin by various technics.

The results of Tunnicliffe's[5] experiments on twenty-four infants and children ranging in age from birth to 3 years, indicate that at birth the opsonic power of the blood serum toward streptococci, pneumococci, and staphylococci is a little less than that of adult serum. It falls still lower during the first months of life, and does not equal the opsonic power of adult serum until about the second year; that the phagocytic activity of the leukocytes of infants toward streptococci, pneumococci, and staphylococci follows a course similar to that of opsonic indexes. The leukocytes at birth are a little less active than adult leukocytes. Their activity diminishes considerably during the first months of life and does not reach that of adult leukocytes until about the third year; that the phagocytic power of the whole blood of infants drops decidedly during the first and second months of life and does not reach that of adult blood until about the third year; that during the first and second years of life the anti-infectious power of the blood, as measured by the opsonic power of the serum and the phagocytic power of the leukocytes, is far below that of adult blood; that these results are in accord with Holt's statistics, showing that during the first months of life when the death rate is highest the anti-infectious power of the blood is lowest. Holt's figures referred to are

3. Cobiliner, S.: Sugar Content in Blood of Nurslings, abstr., Am. Jour. Dis. Child., i, 441.

4. Cannata: Epinephrin in Blood of Newly Born, abstr., Jour. Am. Med. Assn., 1915, lxiv, 1883.

5. Tunnecliffe, Ruth: Anti-Infectious Power of Blood of Infants, Jour. Infect. Dis., 1910, vii, 698.

that from 20 to 25 per cent. of all deaths are of infants under one year, and that 55.1 per cent. of the deaths at this time are caused by bacterial diseases.

In an article by Churchill and Clark[6] Delestre is quoted as having examined the blood of twenty-one premature infants, of whom nineteen died, fifteen of the fatal cases showed organisms in the blood, the order of frequency being streptococcus, colon bacillus, staphylococcus, pneumococcus. The authors' results from blood cultures in infants, made post mortem, are as follows:

Twelve days infant, *Staphylococcus aureus-coli,* few streptococci; 8 months' infant, staphylococcus; 4 months' infant, three organisms resembling in all respects *Streptococcus pyogenes, Staphylococcus aureus,* and *Diplococcus lanceolatus;* 4 months' infant, negative; 3 months' infant, *Staphylococcus aureus, Streptococcus pyogenes;* 6 month's infant, *Staphylococcus albus;* 5 months' infant, *Staphylococcus albus;* 3 months' infant, streptococcus; 3 months' infant, streptococcus; 6 months' infant, negative. The authors recommend that more blood cultures be made in infants as such good results have occurred in adults.

Wollstein and Morgan[7] claim that blood for bacteriologic examination is readily obtainable from the external jugular vein in infants as young as 10 days of age. Their figures are as shown in Table 1.

Polymorphonuclear leukocytes[8] are endowed with proteolytic ferments, and oxidases; the lymphocyte is without either of these; both, however, carry an equal amount of iron.

Schloss[9] quotes the following percentages of eosinophilia averaged from examination of five 1 to 6 months old infants and five 6 to 12 months old infants who were not acutely ill, had hemoglobin more than 50 per cent. and who suffered from no condition recognized as a cause for eosinophilia. For infants from 1 to 6 months old maximum percentage of eosinophils 9.35 per cent., minimum 0.35 per cent., average 3.59 per cent.; for infants from 6 to 12 months, maximum 2.85 per

6. Churchill and Clark: Bacteriology of Blood in Early Life, Am. Jour. Dis. Child., 1911, i, 193.

7. Wollstein and Morgan: Blood Cultures During Life in Infants and Young Children, with Description of Technic, Am. Jour. Dis. Child., 1912, iv, 197.

8. A Comparison of Leukocytes and Lymphocytes, Current Comment Department, Jour. Am. Med. Assn., 1914, lxii, 1261.

9. Schloss: Normal Percentages of Different Varieties of Leukocytes in Infants and Children, Arch. Int. Med., 1910, vi, 638.

cent., minimum 0, average 0.76 per cent. These findings indicate remarkable oscillation. He states that Rosenstern found the eosinophils above 3 per cent. in none of six normal, breast-fed infants, but that in artificially fed infants, the percentages varied from 0.7 to 4 per cent. Schloss' own figures are as given in Table 2, each figure representing the result of five separate counts.

The highest percentages were in infants from two days to two weeks old. He calls attention to the pronounced variations in percentages of the different varieties of leukocytes in apparently normal

TABLE 1.—Bacteria in Blood of Infants

Age	Organism	Age	Organism
7 months	Streptococcus	9 months	None
7 months	None	10 days	None
4½ months	None	2 months	Streptococcus
5 months	None	8 months	None
8 months	Pneumococcus	8½ months	Klebs-Loeffler
2½ months	None	6 months	Pneumococcus
3 months	None	12 months	None
10 days	Aurococcus	10 months	Pneumococcus
8 months	None	6 months	None
9 months	None	2 months	Streptococcus
9 months	Pneumococcus	7 months	Streptococcus
4½ months	None	6 months	Pneumococcus
7 months	None	10 months	None
9 months	None	9 months	Pneumococcus
11½ months	None	5 months	None
6 months	Streptococcus	2½ months	Pneumococcus
9 months	None	8 months	None
9 months	Pneumococcus and B. Influenza	3 months	None
		5 months	Pneumococcus
2½ months	Pneumococcus	12 months	None
4 months	None	7½ months	None
6 months	None	7 months	None
10 months	None	2 months	None
5 months	Pneumococcus	7 months	None
9 months	Pneumococcus	7½ months	None
2½ months	None	2 months	Streptococcus

infants, and that there is a uniform increase of polymorphonuclear cells and decrease of lymphocytes with advancing age. In apparently normal infants, the eosinophils were frequently above the percentages normal for adults, but rarely above 5 per cent. and never above 6 per cent.

Mitchell[10] studied fifty bottle-fed infants, making more than 700 blood counts, thirty-eight of which children were under one year.

10. Mitchell: Leukocyte Count During Digestion in Bottle-Fed Infants, Am. Jour. Dis. Child., 1915, ix, 358.

The method of study was to make a leukocyte count immediately before feeding, one immediately after feeding, one fifteen minutes after feeding, one a half hour after feeding, one an hour after, one an hour and a half after, and so on every half hour until next feeding. This group of counts constitutes a series. Of these series he reported 120. The infants were all bottle fed and while not exactly normal, were of the type usually seen in a hospital, ready for discharge. They were

TABLE 2.—Maximum, Minimum and Average Eosinophilia in Infants from Two Days to Twelve Months Old

Age	Per Cent. Polymorphonuclear Neutrophils	Per Cent. Lymphocytes	Per Cent. Large Mononuclears and Transitionals	Per Cent. Polymorphonuclear Eosinophils	Per Cent. Mast Cells
Two days to two weeks	40.2	55.9	16.2	9.7	0.5
	26.6	47.9	5.1	3	0
	31.9	52.2	9	6	0.1
Two to four weeks	37.5	61.9	13.4	6.8	0.8
	19.5	51.3	3.6	2.6	0
	29.2	55.6	9.7	4.5	0.4
One to two months	37.4	59.1	13.2	7.3	0.9
	22.3	51.1	10.3	5	0.1
	29.7	51.3	11.7	6	0.4
Two to six months	33.4	65.8	13.5	4.5	0.6
	19.5	54.3	6.4	1	0
	25.9	60	10.9	2.5	0.3
Six to twelve months	35.9	58.5	12.2	4.5	0.8
	24.6	50.5	7.3	0	0.1
	30.4	55.9.	9.6	2.6	0.4

all a little under weight. The results of his study show that leukocytosis occurred constantly after feeding in only 12 per cent., although in 32 per cent. it occurred occasionally, and in 56 per cent. leukopenia occurred constantly. In the 120 series 28.3 per cent. showed leukocytosis and 68.3 per cent. leukopenia, leaving 3.3 per cent. so irregular as to be indeterminable. The decrease is greatest at from one to two and a half hours after feeding, and tends to rise before next feeding. When increase does occur it is most frequently seen after feeding and

begins to decline in a half hour. Crying, struggling, and chilling of the part from which the blood is extracted increases the count.

Hess[11] reports marked leukocytosis with moderate but absolute lymphocytosis in all his cases of epidemic meningitis; the neutrophil predominated before the administration of serum; eosinophils disappeared early in the infection, but recurred as convalescence set in; at no time did there exist marked eosinophilia. Leukocytosis in pneumonia varied as to severity of infection and resistance of patient; young infants who reacted well showed neutrophilia and moderate lymphocytosis before the crisis; neutrophils decreased in number after the crisis.

Lucas[12] says that a reversal of the blood picture normal to infants usually occurs about a week before any visible symptoms of infection, such as coryza, Koplik's spots, or coughing, occur; that such a reversal is always present at least forty-eight hours before these symptoms. The picture normally, he says, shows from 50 to 70 per cent. lymphocytes, from 25 to 30 per cent. neutrophils, and from 8 to 15 per cent. large mononuclears. Although there is an actual diminution of the number of neutrophils, there is a relative increase, due to the still more marked leukopenia which precedes the physical signs of measles by eight days. Accompanying this change is an ever-increasing number of disintegrated cells, with abundant granulations separating from the nuclei.

Kolmer[13] gives a summary of blood examination of normal institutional children which he considered a normal standard after examining the blood of a large number of institutional children and which he used for comparison in examining the blood of unknown children of similar age. For the age of 3 months to 1 year, it is leukocytes 10,000, large lymphocytes, 45.57 per cent., small lymphocytes 13.53 per cent., transitionals 2.02 per cent., polymorphonuclears 36.78 per cent., eosinophils 2.13 per cent., mast cells 0.07 per cent.

Finkelstein[14] remarks that some infants whose pallor would suggest anemia show a normal blood count and picture; but that some infants

11. Hess: Leukocyte Counts in Pneumonia and Cerebrospinal Meningitis, Am. Jour. Dis. Child., 1914, vii, 1; abstr., Jour. Am. Med. Assn., 1914, lxii, 328.

12. Lucas, W. P.: Value of Blood Picture in Early Diagnosis of Measles, Am. Jour. Dis. Child., 1914, vii, 149; abstr., Jour. Am. Med. Assn., 1914, lxii, 644.

13. Kolmer: Diagnostic Value of Blood Examination in Pertussis, Am. Jour. Dis. Child., 1911, i, 431.

14. Finkelstein, H.: Anemia in Infants, Berl. klin. Wchnschr., Oct. 9, 1911; abstr., Jour. Am. Med. Assn., 1911, lvii, 1648.

are born without the normal reserve of iron which in normal infants bridges over the nursing period until iron-containing food is included in a general mixed diet. This most frequently occurs in premature infants, in twins, or in the progeny of anemic, neuropathic mothers. He believes that pseudoleukemic anemia of infants is an extreme type of secondary anemia from toxic or infectious causes in children with congenital debility of blood-producing organs, and that its prospect, therefore, for cure is good if the infant is kept in pure air and free from complications, with proper care and diet.

Mason[15] of Baltimore reported a case of a 9-months-old girl with leukocytosis of 200,000, atypical granulations seen with neutrophilic myelocytes, as well as eosinophilic and basophilic myelocytes. There was no enlargement of glands or spleen; no necrosis or hemorrhage of mucous membrane. The course of the disease was three weeks.

A girl infant of 17 months had the highest leukocyte count Veeder[16] was able to find in lymphatic leukemia of childhood. The count was leukocytes 1,330,000, erythrocytes 3,370,000, hemoglobin 55 per cent., lymphocytes 98.5 per cent., polymorphonuclears 1.2 per cent., myelocytes 0.3 per cent.

Emerson[17] says that Gundobin, Carstarjen and Warfield report that on the first day after birth the average leukocytosis is about 26,000; on the third day 13,270; on the eleventh day 15,740. The first few days occurs an absolute increase in the polymorphonuclear neutrophils (70.42 per cent. the first day, 53.16 per cent. the second day, 34.2 per cent. the eleventh day); the large mononuclears and transitionals are high, being 10.76, 16.67, and 15.98 per cent. respectively on these three days; the eosinophils vary much; mast cells and myelocytes are rare; the count usually considered normal for infants (40 per cent. small mononuclears), does not occur until the eleventh day. This leukocytosis has been explained as a concentration of the blood, or a digestion leukocytosis, but the more rational explanation is the rapid blood formation at this age. Although normal infants vary much, yet this rather high count may continue until from the third to the sixth year. During these early years the small mononuclears vary from 40 to 60 per cent., the polymorphonuclear neutrophils from 18 to 40 per cent..

15. Mason: Case of Myelogenous Leukemia in Infant Nine Months Old, Society Proceedings Department, Jour. Am. Med. Assn., 1915, lxiv, 2167.

16. Veeder: Acute Lymphatic Leukemia in Infant, Arch. Pediat., abstr., Jour. Am. Med. Assn., 1911, lvi, 620.

17. Emerson: Clinical Diagnosis, 1913.

with often a slight increase in eosinophils. Digestion leukocytosis is greatest in the infant after his first meal of cow's milk, for the nursing infant it is said to be absent.

According to Wood[18] in children under 1 year the relationship of mononuclear to polymorphonuclear cells is often inverted, as compared to that of adults, being about two to one. During the nursing period the average number of red cells is higher than in adults, being about 5,580,000, with a maximum during the first week of life. Physiologic variations in successive counts are frequently met with in nurslings, fluctuations of a million cells being occasionally found. The hemoglobin is high for a few days after birth, and then sinks, so that it is lower in the first year of life than later, and also shows considerable variations, the percentage varying from 58 to 78 per cent. In infants during the first few days after birth the specific gravity undergoes rapid fluctuations between 1.06 and 1.08, probably due to venous stasis at the time of delivery and the chilling of the body afterward. The density of the blood does not correspond either with the hemoglobin or with the number of corpuscles. After this time the variations are less irregular and in the first few months the specific gravity fluctuates between 1.055 and 1.059. During the first few days after birth the leukocytes may reach 15,000 to 19,000, while in the nursing period they average 12,000. In the blood of healthy nursing infants up to the age of about 8 months, it is possible after prolonged searching to find occasional nucleated red cells of two types; one in which the cell is about the same size as that of the normal red cell, usually with a pyknotic nucleus and an orthochromatic cell body; the other from two to four times as large as the normal red cell and with a polychromatic cell body and a nucleus showing a distinct chromatic network. During the nursing period, the relative proportion of the lymphocytes varies from 51 to 59 per cent., while the proportion of neutrophils is about 28 per cent. From the eighth to the tenth month an increase in the absolute and relative number of the lymphocytes is noticeable, the proportion rising to 61 per cent. After the tenth month a fall is again noted to 56 per cent., the neutrophils slightly increasing during this period to 34 per cent. Transitional neutrophils are present during the first few months up to about 11 per cent., but fall gradually to about 7 per cent. by the end of the first year. The eosinophils vary from 7.5

18. Wood: Chemical and Microscopical Diagnosis, 1911.

to 0.5 per cent. during the nursing period. The large lymphocytes are usually more abundant than in adults.

Gulland and Goodall[19] state that at birth the number of red corpuscles is very high, about 6,000,000 per cu. mm. Hemoglobin is also high, being about 120 per cent.; not infrequently the color index tends to be high from the fact that the corpuscles, like those of fetal life, are larger than in adult life. There is slight variation in the size of red cells and in some healthy infants there may be a slight degree of polychromasia. Nucleated red cells (normoblasts) are always present in the circulation of infants for some time after birth. They are quite numerous the first hours, gradually diminish and are difficult to find after seven days. The polycythemia soon disappears and normal count is reached in two weeks. Hemoglobin falls gradually throughout infancy to about 80 per cent. Leukocytes at birth are numerous, about 18,000, increase a little for two days, may reach 30,000, then rapidly decrease to about 10,000 by the first week, after this they again increase. At 8 months, they are about 15,000; at 12 months about 10,000. The variations of the first week are variations of polymorphonuclears, which may reach a maximum of 70 per cent. and fall to 20 per cent. During the remainder of infancy and until the fourth year, the lymphocytes predominate, being about 60 per cent. This percentage is still higher if development be delayed or nutrition impaired. The leukocytes are more responsive to stimuli in infants than in adults.

As the result of our study of the foregoing literature we decided to limit our work to the relative percentage of the white cells, as there were only two articles dealing with this particular phase of the subject, the first being by Schloss.[20] He calls attention to the pronounced varieties in the percentage of the different varieties of leukocytes in apparently normal infants. This is in line with our experience. His percentage of eosinophils averaged higher than in our series. As it will be noticed that in a number of infants, none of these cells appeared. The second article is by Mitchell,[21] who studied the leukocyte count during digestion in bottle-fed infants. He studied fifty infants, making a count every half hour after every feeding until the next feeding. His conclusions were that leukocytosis occurred constantly in only

19. Gulland and Goodall: The Blood. 1912.
20. Schloss: Arch. Int. Med., 1910, vi, 658.
21. Mitchell: Jour. Dis. Child., 1915, ix, 358.

TABLE 3.—The Fifty-One Counts Made by Dr. A. A. Johnson

Name	Age, Mo.	Small Lymphocytes	Large Lymphocytes	Polymorphonuclears	Transitionals	Eosinophils
Violet	11	20	44	28	8	..
Billy	9	12	31	40	7	2
Dorothy	2	21	38	31	8	2
Indian (1)	9	16	31	49	4	..
Thurston	12	28	39	29	4	..
Carak	2	18	37	41	3	1
Charles	11	30	36	32	2	..
Viola	11	20	49	21	8	2
Henry	12	25	30	40	3	2
John	3	19	35	39	7	..
Indian (2)	5	22	38	35	5	..
Billy	9	20	31	40	8	1
Leslie	3	48	20	22	9	1
Robert	4	16	41	33	8	2
Elmer	12	24	36	37	3	..
Anderson	6	14	39	41	6	..
Edward	1	19	31	43	7	..
Anna	2	27	40	30	3	..
Martha	12	19	29	40	2	..
Eva	3	23	31	37	8	1
Mary	3	19	40	38	3	..
Isabel	¾	16	26	48	8	2
Helen	1	27	43	26	4	..
Evelyn	4	22	28	43	5	2
Naomi	12	30	26	34	7	3
Morris	12	14	41	35	7	3
Romona	2	22	41	37	9	1
Roy	1	12	32	46	7	3
Wama	1	25	41	30	4	..
William	12	33	48	34	5	..
Rosy	8	15	55	23	7	..
Abe	3	20	57	17	6	..
Leroy	12	32	29	38	7	..
Edward	6	21	46	28	4	..

TABLE 3.—The Fifty-One Counts Made by Dr. A. A. Johnson—(*Continued*)

Name	Age, Mo.	Small Lymphocytes	Large Lymphocytes	Polymorphonuclears	Transitionals	Eosinophils
Lesley	4	14	33	43	8	2
May	¾	21	42	28	9	..
Joe	12	19	51	25	5	..
Ardeth	2	26	43	24	7	..
Allen	12	36	41	19	4	1
Abner	3	20	33	41	5	1
Ira	4	40	18	29	12	1
Hudson	6	22	33	39	4	2
Westley	2	28	36	27	9	..
Private	6	25	32	41	2	..
Morgan	12	14	65	25	3	1
Stanley	9	36	31	28	4	1
Stanford	9	10	50	35	5	0
Lewis	12	15	65	15	5	0
Christie	12	22	54	20	4	0
Monroe	7	22	51	17	10	0
Furnas	8	14	60	20	16	0

12 per cent. of the cases. In 32 per cent. it occurred occasionally, and in 56 per cent. leukopenia occurred constantly.

The laboratory work was done by Prof. A. A. Johnson, M.D., instructor in bacteriology, medical department, Nebraska University, and Clyde Moore, M.D., instructor in pediatrics. My work consisted in the examination of the infants before the tests were made and also keeping them under observation for at least two weeks afterwards, to determine the physical condition of the infants. Dr. Johnson made counts on fifty-one infants and Dr. Moore on thirty infants, making a total of eighty-one, ranging in age from 3 weeks to 1 year. From this there is eliminated ten infants on whom the count was made by the above Drs. Moore and Johnson, each working independently of the other. Three others were eliminated because they showed symptoms of acute infection three days after the blood count, leaving a total of sixty-eight. It will be noticed that there is a wide discrepancy between the count of the large and small lymphocytes by the two observers.

This is due to the fact that Dr. Johnson called all white cells small that had a small amount of cytoplasm, without regard to the size of the cell, after the manner of Pappenheim, while Dr. Moore assumed that all white cells not larger than a red cell were small, without regard to the amount of cytoplasm. All of the above infants were in average health at the time the blood was taken. That is, they were gaining in weight, had normal stools and were free from any evidence of acute or chronic disease. All were bottle-fed infants, all received modified milk made from certified milk.

METHOD OF PROCEDURE

The method of procedure was simply to make a puncture, procure a drop of blood on the slide, at once spread by means of another slide, then dry and stain with Jenner's stain. The differential count of the whites was then made by passing the slide across the field of the objective, the count being made in series of 100. The result of the

TABLE 4.—The Seventeen Counts Made by Dr. Clyde Moore

Name	Age, Mo.	Small Lymphocytes	Large Lymphocytes	Polymorphonuclears	Transitionals	Eosinophils
Leo	10	3	66	22	3	6
Ardiff	2	35	12	49	2	2
Iola	2	70	11	15	1	3
Romana	2½	80	7	10	1	2
Theodore	2½	80	4	10	4	2
Cecil	4	74	4	15	6	1
Emma	4	84	5	6	2	3
Abraham	3	70	5	21	4	..
Bobbie	12	62	5	30	2	1
Eddie	1½	88	2	8	2	..
Marlan	¾	62	9	23	6	..
Eleanor	2½	75	8	13	1	3
Alvin	2	77	4	13	2	4
Ellen	1½	62	5	22	3	3
Marie	¾	64	14	16	2	4
Ray	1	59	7	29	3	2
Rubert	3½	82	2	15	0	1

examinations of Drs. Johnson and Moore is shown in Tables 3 and 4, respectively.

In the lists given in Tables 3 and 4 no infant was under 3 weeks of age or over 12 months.

In view of the fact of the variation of the counts of the large and small lymphocytes between the two observers, we have grouped the large and small in one class, as shown in Table 5.

TABLE 5.—Summary of Data in Tables 3 and 4, Arranged According to Age of Subject

Age, Months	Cases	Lympho-cytes	Poly-morpho-nuclears	Trans-itionals	Eosino-phils
Under 2..	20	64	28	5	1
2 to 4	17	69	25	5	1
4 to 6	3	60	35	5	0
6 to 8..	3	55	40	4	0
8 to 10	4	52	41	5	2
10 to 12	14	64	31	5	0

CONCLUSIONS

No new facts were developed. The result of our work shows that the blood of infants varies from that of the adult in the high proportion of the lymphocytes. On May 1 and 2 Dr. Johnson made a second count on fourteen infants in both lists. Comparing these with the first slides of the same infants, we find a considerable variation, so that the blood of the infant varies from day to day in its relative proportion of white cells, and there is a gradual but irregular increase in the polymorphonuclear cells during the first year of life.

DISCUSSION

Dr. Schloss: It is rather surprising how few blood counts have been made on normal children. Very elaborate counts were published ten years ago by Carstanjen, and these are the ones usually quoted. His counts showed the same variation that the author has called attention to. There is great difficulty in establishing an average percentage of white cells, because these cells vary a great deal. If one wants to be absolutely accurate, the blood count of white cells should include at least 500 of these cells, and it is quite a task for a physician to make so large a count. The second source of error is due to differences in classification. It is difficult to tell in what class many cells belong. Also, in many cases, the blood varies from hour to hour, and this produces variations in the count. It is much more accurate to state the max-

imum and minimum count at a certain age than to give a percentage, because the count will vary as much as 10 or 15 per cent. in apparently normal children of the same age.

Dr. Sedgwick: I have found it difficult to obtain normal counts, and Mr. Mitchell, a student in pediatrics at the University of Minnesota, who has done considerable work on the newborn, has made charts of our cases. Repeated counts were made from day to day.

Dr. Cowie: About nine years ago we made a similar investigation at the University of Michigan Hospital. We made differential counts on the mother's blood taken from the umbilical cord just after birth, and blood from the infant daily for fourteen days, the length of time infants remained in hospital after birth. The results were similar to those found out before, that is, similar to those reported by Monti. The observations were carried on as a study to familiarize ourselves with the normal changes in infant's blood, and were not published. The study continued over a period of two years. We were very much interested in the nucleated red cells. In almost all cases examined nucleated red cells had disappeared entirely from the blood by the fourteenth day. There is a very marked tendency for infants' and very young children's blood to revert to the embryonal type on the slightest provocation. The curves shown today remind me very much of those obtained by us.

THE CREATININ AND CREATIN CONTENT OF THE BLOOD OF CHILDREN *

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There are comparatively few data on the creatin-creatinin content of the blood, as it was not until 1914 that a satisfactory method for its determination was devised by Folin.[1] At the same time Folin and Denis[2] reported the results of a number of determinations in adults with different clinical conditions. They found that the blood content of normal adults averaged a little over 1.1 mg. of creatinin per 100 c.c. They were unable to find any specific creatinin retention, but found an increased retention (over 20 mg.) in some cases of nephritis. About the same time Neubauer,[3] in a paper on the use of creatinin as a test of renal function in nephritis, stated that creatinin retention in the blood was very high in some cases of nephritis, reaching 20 mg. per 100 c.c., and that normally it was present in quantities less than 1 mg. per 100 c.c. He gives no other figures.

In two more recent papers Myers and Fine[4] and Myers and Lough[5] report the result of some studies of the creatin-creatinin content of the blood in nephritis. They found, as Folin found, a high retention figure in some cases, but not in all. They noted that all their cases of nephritis with a retention of over 5 mg. of creatinin per 100 c.c. terminated fatally. Of these, there were eleven cases. In all they studied thirty nephritics. In only five patients was the retention under 2 mg. (normal values) and two of these died. From a clinical point of view they consider a case with a creatinin content between 3 and 5 mg. as having

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1. Folin: Jour. Biol. Chem., 1914, xvii, 475.
2. Folin and Denis: Jour. Biol. Chem., 1914, xvii, 487.
3. Neubauer: München. med. Wchnschr., 1914, lxi, 857.
4. Myers and Fine: Jour. Biol. Chem., 1915, xx, 391.
5. Myers and Lough: Arch. Int. Med., 1915, xvi, 536.

an unfavorable prognosis, and those with over 5 mg. as fatal. In a number of normal cases tested they found the creatinin content under 2 mg. per 100 c.c. of blood in almost every case.

The creatinin retention in nephritis is apparently but a part of the general retention of nitrogenous substances in the blood, which has been noted by many observers, and there is a definite parallelism between the creatin retention and the retention of the total nonprotein nitrogen, urea and uric acid. There is no evidence at hand leading one to consider it a more delicate index of retention than any of the other nitrogenous substances, and in fact it seems to be more easily excreted.

In the figures obtained by both of these groups of workers the creatin content varied widely and neither paper discusses the creatin figures. If one studies the tables of Folin and Denis it will be noted that the creatin content of the blood averages about 10 mg. per 100 c.c.

Because of the difference in the creatin-creatinin metabolism in adults and children, as measured by their content in the urine, we decided to test the blood of a number of children with different clinical conditions and compare the results with the total nonprotein nitrogen of the blood.

Folin and Denis[6] found that the content of nonprotein nitrogen in the blood of a healthy adult was from 22 to 26 mg. per 100 c.c. Later they published determinations made in a large number of clinical conditions, which showed that there is a definite increase or retention of the nonprotein nitrogen in nephritics with uremia, and that greater variations are found in the blood of hospital patients. Slightly higher values are not necessarily associated with renal disturbance. These findings have been confirmed by a number of observers. There is an increase of from 4 to 6 mg. after a full meal, and usually a slight increase in acute infections. In nephritics the content may vary from normal to ten times normal, the high values being found in actual or impending uremia.

In children the nonprotein nitrogen content does not differ in any marked degree from the adult. Tileston and Comfort[7] made determinations on fifty-one children with a variety of clinical conditions. Normal children gave values of from 20 to 34 mg. per 100 c.c. Only one case, that of a child with acute nephritis, showed a definitely

6. Folin and Denis: Jour. Biol. Chem., 1913, xlv, 29.
7. Tileston and Comfort: Am. Jour. Dis. Child., 1915, x, 278.

increased value (63 mg. per 100 c.c.), and this later became normal with the disappearance of uremic symptoms. The rest of the observations were made on children with acute and chronic infections, in whom normal values (20 to 32 mg. per 100 c.c.) were found. In normal infants the nonprotein nitrogen content has been found to vary between 23 and 44 mg. per 100 c.c. by Schlutz and Pettibone,[8] whose observations were made on nine infants from ½ hour to 10 days old.

The methods used in our study were those of Folin and Denis[9] for the nonprotein nitrogen and of Folin[1] for the creatin and creatinin. In the latter test the blood was laked in distilled water before shaking with picric acid, instead of being laked in a saturated solution of picric acid. Five c.c. of blood were used in determining the nonprotein nitrogen (N. P. N.) and 6 c.c. for the creatinin ($Cr._1$) and creatin ($Cr._2$) determinations. All figures are for milligrams in 100 c.c. of blood.

Determinations were made on seventy-five children. Many of these, particularly those with scarlet fever, were tested a number of times. In order to avoid any factor which might result from the ingestion of food, the blood for the tests was taken early in the morning before the children were given their breakfast, and thus about twelve hours after the last meal. The children were placed on a creatin-free diet for the study. In Table 1 the results in seventy-seven tests are tabulated. The cases are grouped into normals; scarlet fever at the time of exanthem, when there was an elevation of temperature; afebrile scarlet fever, in the first week; and a number of examinations made in the third week of convalescence (negative urinary findings). In addition a number of miscellaneous conditions are added.

The creatinin figure for normal children varies between 0.58 and 3.44 mg. per 100 c.c. In ten children the figure was under 2 mg., and in two above. The febrile scarlet fever cases varied between 1.08 and 3.82 mg., but with half above 2 mg. and none under 1. The highest figure in an early afebrile case was 2.78, but in half the cases the content was a little over 2 mg. In convalescence only one case in eleven had a content above 2 mg. Like variations were encountered in the miscellaneous conditions. There was no specific retention in any of our cases, although as a whole the figure for the creatinin content of the blood in children is somewhat higher than that for the adult. A comparison of the creatinin content with the nonprotein nitrogen is briefly

8. Schlutz and Pettibone: Am. Jour. Dis. Child., 1915, x, 206.
9. Folin and Denis: Jour. Biol. Chem., 1912, xi, 527.

TABLE 1.—NITROGEN RETENTION IN CHILDREN IN SCARLET FEVER AND VARIOUS CLINICAL CONDITIONS

Initials	Sex	Age, Years	Condition	Creatinin, C.c.	Nonprotein Nitrogen, C.c.	Creatin, C.c.
A. C.	♀	2	Normal	1.41	22.0	7.17
C. H.	♀	3	Normal	1.20	26.0	4.70
B. V.	♂	7	Normal	3.44	26.0	2.77
C. C.	♂	9	Normal	2.80	26.0	4.10
T. H.	♂	12	Normal	2.30	33.0	6.40
N. M.	♀	13	Normal	0.78	29.0	4.92
L. K.	♀	14	Normal	2.30	30.0	4.55
E. B.	♂	5	Normal	0.97	25.0	7.16
M. R.	♀	9	Normal	1.92	27.0	2.95
M. R.	♀	8	Normal	0.90	32.0	2.21
M. K.	♀	3	Normal	0.79	32.0	3.41
C. Z.	♂	8	Normal	2.70	31.0	2.60
H. Z.	♂	5	Normal	0.58	28.0	3.92
C. P.	♂	3	Normal	3.24	28.0	3.22
M. R.	♀	12	Normal	1.00	31.0	3.40
R. D.	♀	2	Normal	0.68	25.0	3.54
E. B.	♂	11	Scarlet fever (febrile): Severe	3.44	31.0	3.16
F. S.	♂	5	Mild	1.38	29.0	5.28
A. C.	♂	4	Severe	1.62	22.0	5.53
D. B.	♂	2	Severe	2.38	34.0	1.85
M. M.	♀	8	Mild	1.42	28.0	2.97
I. M.	♀	6	Mild	1.82	27.0	3.23
I. H.	♀	4	Mild	1.08	16.0	....
M. I.	♂	6	Mild	2.79	29.0	2.58
J. W.	♂	11	Mild	1.77	35.0	3.73
A. F.	♂	6	Mild	1.61	32.0	4.11
H. B.	♂	1⅔	Severe	3.82	26.4	4.12
O. B.	♂	3	Severe	2.03	21.5	3.91
A. M.	♀	5	Severe	2.32	29.0	3.14
B. S.	♀	4	Severe	1.91	21.0	2.62
I. F.	♂	4	Severe	3.00	25.0	2.38
L. M.	♀	12	Scarlet fever (afebrile): Early	1.87	19.0	5.67

TABLE 1.—NITROGEN RETENTION IN CHILDREN IN SCARLET FEVER AND VARIOUS CLINICAL CONDITIONS—(*Continued*)

Initials	Sex	Age, Years	Condition	Creatinin, C.c.	Nonprotein Nitrogen, C.c.	Creatin, C.c.
A. F.	♂	2½	Early	1.43	30.0	3.84
M. E.	♀	3	Early	2.38	18.0	3.41
L. O.	♂	10	Early	2.12	19.0	4.06
			Scarlet fever (afebrile):			
S. M.	♂	3	Early	2.78	18.5	3.17
W. J.	♂	6	Early	2.20	33.0	3.68
E. W.	♂	4	Early	2.27	14.5	3.78
C. L.	♂	7	Early	2.36	30.0	2.51
G. N.	♀	8	Early	1.06	25.0	3.94
H. B.	♀	9	Early	1.33	23.0	2.29
			Reexamined (3d week):			
J. W.	♂	11	" "	1.34	32.0	4.51
A. F.	♂	6	" "	1.28	20.0	4.85
M. I.	♂	6	" "	2.80	29.0	5.53
H. B.	♀	9	" "	1.62	22.5	4.63
G. N.	♀	8	" "	1.21	21.7	3.97
I. M.	♀	6	" "	1.44	24.0	4.06
M. M.	♀	8	" "	1.27	22.4	3.44
I. H.	♀	4	" "	0.62	27.0	4.80
C. L.	♂	7	" "	0.94	21.6	3.22
H. C.	♂	5	" "	1.90	22.3	3.41
F. S.	♂	5	" "	1.00	24.5	4.21
			Congenital heart disease:			
M. S.	♀	9	Pulmonary stenosis	0.99	33.0	2.80
F. B.	♂	1	Pulmonary stenosis	0.74	29.0	....
R. R.	♀	8	Chorea	2.50	26.0	4.50
Mc. G.	♂	9	Typhoid conv.	3.22	30.0	4.53
			Nephritis:			
R. C.	♂	3	Acute	1.46	23.0	....
M. D.	♀	3	Chronic diffuse	2.52	42.0	7.20
L. V.	♂	8	Chronic diffuse	2.07	20.0	....
K. P.	♂	1⅓	Acute (mild)	1.21	36.0	5.28
V. R. 1/17	♀	6	Acute (severe)	0.80	39.0	....
V. R. 1/28	..	..	Severe	1.66	49.0	....
V. R. 3/15	..	..	Severe	1.77	18.0	....

TABLE 1.—NITROGEN RETENTION IN CHILDREN IN SCARLET FEVER AND VARIOUS CLINICAL CONDITIONS—(*Continued*)

Initials	Sex	Age, Years	Condition	Creatinin, C.c.	Nonprotein Nitrogen, C.c.	Creatin, C.c.
V. R. 4/S....	..	..	Severe.....	0.98	21.7	....
R. K.....	♂	11	Tuberculosis, open pulmonary..	1.67	23.0	10.00
L. O. N.....	♂	13	Tuberculosis, open pulmonary..	0.71	32.0	5.00
L. S.....	♀	6	Tuberculosis, open pulmonary..	1.40	35.0	5.50
M. S.....	♀	5	Tuberculosis, open pulmonary..	1.78	40.0	3.68
M. H.....	♂	14	Anemia, malarial.....	0.83	49.0	6.74
W. P.....	♂	11	Anemia, secondary.....	1.54	25.8	....
M. B.....	♀	10	Myocarditis.....	0.76	24.0	4.78
L. C.....	♂	8	Cardiac decompensation.....	3.20	29.0	2.20
H. S.....	♀	9	Chronic bronchitis.....	1.60	24.0	2.25
M. N.....	♀	7	Chronic bronchitis.....	1.71	40.0	4.53
S. F.....	♂	1	Chronic bronchitis.....	1.49	32.0	4.15
H. K.....	♀	⅔	Chronic malnutrition.....	2.85	20.0	3.00

shown in Table 2, in which the cases are grouped according to the amount of each present.

Under 30 mg. of nonprotein nitrogen and 2 mg. of creatinin are considered as corresponding to average normal figures and hence are grouped together. In Group 2 are cases with a figure of from 30 to 35 mg. of nonprotein nitrogen and from 2 to 3 of creatinin per 100 c.c.; Group 3, from 35 to 40 of nonprotein nitrogen and from 3 to 4 of creatinin; Group 4, over 40 mg. of nonprotein nitrogen and 4 of creatinin.

In addition, the nonprotein nitrogen and creatinin were both in Group 2 in two cases each of congenital and of chronic valvular heart disease and in a case of myocarditis. In a child with secondary anemia and in one who had been starved for two days the nonprotein nitrogen was high (over 40), while the creatinin was low. In a typhoid convalescent, in a child with cardiac decompensation and in one with chorea the creatinin figure was in a higher group. As a rule both the nonprotein nitrogen and the creatinin were within the same general limits as have been found for normal adults, and as Tileston found for

the nonprotein nitrogen in children, although as a whole the average figures for both are a little higher in children.

We have been able to study but six cases of nephritis. The retention figures in these were not high and but one case was fatal (not

TABLE 2.—COMPARISON OF CREATININ AND NONPROTEIN NITROGEN CONTENT IN VARIOUS CLINICAL CONDITIONS

	Group 1		Group 2		Group 3		Group 4	
	Non-protein Nitrogen	Creatinin	Non-protein Nitrogen	Creatinin	Non-protein Nitrogen	Creatinin	Non-protein Nitrogen	Creatinin
Normal	11	10	5	4	..	2	..	..
Scarlet fever	11	8	4	4	..	3	..	..
Scarlet fever (afebrile)	17	14	4	7	..	..	..	..
Tuberculosis	1	4	..	..	2	..	1	..
Nephritis	2	3	..	3	2	..	2	..

uremic). As noted in Table 1 the nonprotein nitrogen was not increased in two cases and the creatinin was normal in three. In one case with a low nonprotein nitrogen figure the creatinin was high and in two an opposite condition held. As the nephritis in a given case subsides the amount of retention decreases, as illustrated by the case shown in Table 3.

TABLE 3.—DECREASE OF NITROGEN RETENTION WITH SUBSIDENCE OF NEPHRITIS

Date	Non-protein Nitrogen	Creatinin	Creatin
1/17/16	39	0.80	5.45
1/28/16	49	1.66	4.55
3/15/16	18	1.77	4.61
4/ 8/16	22	0.97	5.15

A number of cases of scarlet fever were followed from the stage of the acute exanthem until desquamation was completed and tests made weekly for five weeks. None of the fourteen cases followed

developed a typical postscarlatinal nephritis in the third or fourth week. After the acute febrile period was over, there was usually a slight fall in the nonprotein nitrogen and creatinin, although in the second week a few showed a slight increase. One severely toxic patient, who died in the third week, showed an increasing retention. The kidney in this case showed acute fatty degeneration.

Although as stated there was no discussion of the creatin figures in the earlier papers, a study of Folin's tables shows that in a general way the creatin of the blood of adults averages about 10 mg. per 100 c.c. There is no apparent relationship between the amount of creatin and creatinin. We found much less creatin in the blood of children, rarely over 5 mg. per 100 c.c., and the figure for the total creatin-creatinin was rarely over 6 mg. This is interesting in view of the fact that creatin is found in the normal urine of children and is not present in

TABLE 4.—Increasing Nitrogen Retention with Progressive Postscarlatinal Nephritis

	Nonprotein Nitrogen	Creatinin
First week	28	1.51
Second week	34	2.38
Third week	47	....

the urine of adults. We have been unable to find any specific relationship in our figures between the creatinin and creatin, or any relation between the amount of creatin and the clinical condition. There is no definite relation between the total nonprotein nitrogen and the creatinin-creatin content.

A few experiments were made to observe the influence of certain factors on the nonprotein nitrogen and creatinin content. In one the effect of copious water drinking to flush the kidneys was tried. A fixed diet was given for six days. On the first three days but 200 c.c. of water was allowed, on the fourth and fifth, 2,000 c.c. and on the sixth day 3,000 c.c. Determinations were made on the morning following the last five days. The effect was negligible, as is shown by the figures in Table 5.

Determinations were also made on a child who was being starved for other purposes. A slight increase in the content of all three sub-

TABLE 5.—EFFECT OF COPIOUS WATER DRINKING ON NITROGEN RETENTION

Water Daily, C.c.	Nonprotein Nitrogen	Creatinin	Creatin
200	28.0	1.18	3.38
200	23.8	2.00	3.24
2,000	25.7	1.41	3.60
2,000	26.0	1.33	3.42
3,000	22.5	1.15	....

TABLE 6.—EFFECT OF STARVATION ON NITROGEN RETENTION

Day	Diet	Nonprotein Nitrogen	Creatinin	Creatin
1	Regular	31	1.39	4.86
2	Starvation	34	1.67	3.97
3	Starvation	35	1.70	6.70
4	Regular	31	1.36	4.10
5		..	....	....
6	Regular	..	1.24	3.56

TABLE 7.—NITROGEN CONTENT OF BLOOD AND URINE ACCOMPANYING CREATIN-FREE DIET

Blood, Mg. N per 100 C.c.			Urine, Total N		
Nonprotein	Creatinin	Creatin	Total Nitrogen Grams	Creatinin Mg.	Creatin Mg.
L. O'N.*					
17.8	0.84	4.60	7.32	541	59
21.9	0.67	3.78	5.82	476	12
22.1	1.90	4.70	5.46	379	82
22.8	1.46	4.57	....	...	...
21.5	2.04	3.52	6.67	542	83
W. P.†					
26.7	1.33	....	3.54	330	95
25.8	1.54	....	3.24	312	123
21.3	1.54	....	3.72	333	270
27.0	1.25	....	3.63	381	206

* Fourth week of mild scarlet fever.
† Secondary anemia.

stances was observed during the period of starvation. An increased creatinin excretion in the urine occurs during starvation.

Several children were placed on a fixed creatin-free diet for six days and analysis of both the urine and blood made daily after the second day. The figures obtained in two cases are given in Table 7.

In the first case both the absolute and relative (percentage relation to total nitrogen) amount of creatinin of the blood varied considerably, while in the second it is quite uniform. In the first case, as in others, there seems to be no definite relationship between the creatin of the blood and of the urine, or between the quantities of total creatin-creatinin.

The second case is given to show the very slight daily fluctuation of creatinin sometimes observed. What mechanism controls the relation between the amount in the blood and the quantity of the urine we were unable to ascertain. The amount of creatin-creatinin to total nonprotein nitrogen in 100 c.c. of blood is much greater than the proportion of creatinin to total nitrogen of the urine.

THE HOSPITAL CARE OF PREMATURE INFANTS*

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At the outset I wish to say that this is not a general discussion of the topic, but a résumé of my personal experience in the observation and treatment of these cases.

In the past two years there have been admitted to the infants' ward of Bellevue Hospital 278 premature infants. Of these thirteen are still in the warm ward specially provided for premature infants and 265 have been discharged. There are three reasons for the very large number of this class of patients admitted to Bellevue: first, because there is a large maternity ward on the floor just above the infants' wards; second, because Bellevue is a city institution to which the police department brings all the foundlings, and third, because the hospital is known to have special facilities for taking care of these tiny patients. There is, so far as I know, no other institution, either here or abroad, that has so many such cases.

These mites are brought to us in the most diverse and curious wrappings; some beautifully swathed in cotton and warm flannels, with hot water bottles around them, and many others stiff and blue from exposure and insufficient covering. Naturally, many of the latter have received so severe a shock that the small spark of life cannot be fanned into a sufficient flame; it flickers for a day or so and then goes out. This means that the mortality is very high, and the most of it during the first few days after admission to the hospital. But a great deal can be done for even the smallest and feeblest of them, and it is on this account that a consideration of the measures we have found most useful may be of interest to all who are called on in private work to care for these interesting little patients.

I have recently gone through the records of the last 200 patients discharged and find that there were thirty saved, discharged cured, as we say; that is, they were discharged from the hospital in strong

* From the Infants' Service, Bellevue Hospital, New York.

enough condition and with sufficient weight to make it probable that their mothers could care for them successfully. Of the 170 that died in this last 200 patients ninety died on the first day, many within an hour or so of the time of admission; twenty-eight more died on the second and third days, making 118 that died in the first three days. This means that there were thirty that lived out of the eighty-two strong enough to survive the first three days of life, that is, 36 per cent. were saved of those that survived beyond three days. Of those that died, the baby with the highest admission weight was an infant weighing 4 pounds 14 ounces. This baby died of general septicemia. One baby reached 4 pounds 10 ounces and died of gastro-enteritis. Another gained from 2½ pounds up to 4 pounds and then died of acute bronchitis. Still another gained from 2 pounds 3 ounces, its admission weight, to 4 pounds 11 ounces, then it had an infection and died in a few days, much to our chagrin. The lowest weight of those that died was 1 pound 1 ounce, that of an infant of five and a half months' uterogestation. There were many that weighed from 1 pound 12 ounces to 2¼ pounds.

TABLE 1.—Length of Babies of Various Weights, on the Average

Weight, Pounds	Length Inches	Length, Cm.	Weight, Pounds	Length, Inches	Length, Cm.
7½	11 to 12	28 to 31	4	16½ to 18	42 to 46
2	13½ to 14½	34 to 36	5	18 to 19	45 to 48
2½	14 to 15½	36 to 40	6	19 to 20	48 to 51
3	15 to 16	38 to 41	7	20 to 21	50 to 54
3½	15½ to 16½	39 to 42			

The smallest infant that was discharged cured had an admission weight of 2 pounds 13½ ounces. The baby remained in the hospital seven months and weighed 5 pounds 6½ ounces at the time of discharge. The next smallest baby that was discharged cured weighed 3 pounds on admission and after four months in the hospital was discharged weighing 5 pounds 5 ounces.

Three years ago, while visiting the children's clinics on the Continent, I learned that in Paris the smallest premature infant they had reared successfully weighed 800 gm., and in Berlin at Langstein's Hospital an infant of 750 gm., a case of L. F. Meyer, had been suc-

cessfully reared. It is most unusual, however, that any baby weighing less than 2½ pounds is saved. The smallest child reported saved is that of Rodmann, weight 719 gm.

The great majority of the babies admitted to the premature ward have a history of uterogestation between seven and seven and a half months. But it must be emphasized that the history is not to be depended on. In our experience, in cases in which the history has seemed more than usually reliable, babies of six months' uterogestation weighed from 1½ to 2 pounds; those of seven months weighed from 2¾ to 4 pounds, and those of eight months weighed from 4½ to 5½ pounds.

These are to be taken only as general averages; there are many exceptions, both in the direction of the earlier born, weighing more than these figures, and of the later born, weighing less. This is particularly true in the case of multiple births, such as twins or triplets.

Causes of Prematurity.—Aside from mental or physical shock, the result of an accident, the causes of prematurity are, briefly, syphilis, some acute disease in the mother, extreme youth of the mother or of both parents, and, connected with this, illegitimacy. The occurrence of twins or triplets or other multiple pregnancies is a very important factor.

Symptoms.—Aside from the small size and weight of the premature baby, the usual symptoms manifested are, in the first place, extreme muscular feebleness, which extends even to the muscles involved in sucking and swallowing. Inability to nurse, that is, to make sufficiently strong suction to withdraw the milk from the mother's breast, is the regular condition, and in very many instances it is the underlying cause of fatal inanition; that is to say, the mother may, after a few days, have abundant, normal milk and the baby may have a good digestion, but on account of feebleness of its muscular power the baby is unable to obtain the nourishment.

Another symptom manifested by nearly all of these babies, partly on account of their small size, but for other reasons which will be mentioned, is a temperature far below normal. The skin is imperfectly developed and the subcutaneous fat is deficient or lacking, so that the baby radiates more heat proportionately than an infant of normal size. Again, the heat regulating center seems not to be in satisfactory operation, so that the baby is thermolabile, very susceptible to the heat changes of its environment. With regard to the skin, babies born

very early may have a skin which is partly translucent, having the appearance of solidified gelatin. These babies with gelatinous skin are seldom able to survive.

Another symptom which these babies show is a great tendency to attacks of cyanosis. This in some instances is due to pressure of the clothes or the weight of the arms on the chest, but in other instances it seems to be related to the feeble muscular power and easy fatigue which the muscles of respiration undergo. The attacks may be so serious as to prove fatal, so that constant care is necessary to prevent bad results. Another cause of cyanosis is insufficient food.

These babies also have an extreme susceptibility to all sorts of infection. The skin and mucous membranes are very permeable to germs, so that extreme care is necessary to prevent abrasions and to avoid contagion from other persons or from contaminated clothing or apparatus.

Absorption from the gastro-intestinal tract of deleterious substances, whether as the result of fermentative processes in the intestines or of germ infection, may cause profound and even fatal disturbance in a very short time. General sepsis may arise from this source or may come from the umbilical wound or from abrasions of the skin. On the other hand, occasionally one sees localized infections that cause comparatively little disturbance. This principally occurs in the hands and feet, where the blood supply is very good.

Not always, however, does a serious disease prove fatal to the premature infant. Baby 786, weighing 4 pounds, had an attack of bronchopneumonia, with temperature ranging up to 104 F. for over a week, recovered and afterward gained in weight and was discharged from the hospital in good condition.

TREATMENT

General Management.—So far as is possible it is the aim in the general management of the baby to reproduce the conditions of intra-uterine life, conditions which the baby should have been entitled to until the ordinary full period of intra-uterine development; that is to say, the baby should be kept in an even temperature approximating that of the human body and should be shielded from all sorts of external shocks, whether thermal or mechanical. The skin should be protected from chances of contagion and injury and the eyes should be protected from light. The inhaled air should be moist and compara-

tively warm and as free as possible from germs, and the food should be such as to require the least possible amount of digestive effort on the part of the baby. To secure as far as possible the conditions mentioned, certain specific factors are of the greatest importance. First, *the temperature of the environment*. This is much more readily managed in summer than in winter, but with a little care and attention very satisfactory conditions can be obtained, even in any home. The first question that will arise on the part of the family and the physician in the management of a premature baby is whether or not it should be put into an incubator. My experience with most incubators and their methods of management would lead me to give a decided negative to this question. Incubators are expensive; they are complicated. It is inconvenient to change the baby's clothing while it is in an incubator, and most of all, an incubator is difficult to ventilate and to keep free from germ contamination. Moreover, to keep the temperature equable in them and the ventilation proper requires a nurse who is thoroughly familiar with the use of the particular incubator installed.

As regards incubators, probably the most satisfactory one up to the present time is that devised by Dr. Edwin B. Cragin and described in the *Journal of the American Medical Association* for Sept. 12, 1914. Dr. Cragin devised his incubator to overcome the objections he had to others, namely, insufficient air space, insufficient circulation of air and difficulty of maintaining a constant temperature. Accordingly he made his incubator much larger, holding two basins arranged with electric fan to draw through a current of filtered air and made use of a series of electric bulbs for heating. The air is moistened by evaporation of a pan of water placed in the lower part of the incubator. A thermometer and a hygrometer show the heat and moisture. Altogether, however, there are so many disadvantages in the use of incubators, as compared to their advantages, that the plan of setting aside a small room as an incubator room and having that kept at the proper temperature is much more satisfactory in every way. Here the baby does not have to undergo any chilling when the clothing is removed for any purpose.

The most complete incubator rooms have the air drawn in front doors from some uncontaminated source (in cities usually best from the roof) and it is then warmed, filtered and moistened. The temperature of the room is regulated automatically and the degree of the

heat can be adjusted. Such an installation is quite expensive. The Babies' Hospital in New York has such a room which was installed under Dr. Holt's direction.

TABLE 2.—Premature Infants in Bellevue Hospital, June, 1915, Showing Relation of Weight to Length

Name	Gestation Period, Mo.	Weight, Lb.	Weight, Oz.	Length, Cm.	Length, In.
1. T.	..	3	4½	39	15½
2. J. T.	...	3	2	40.5	16
3. D. C.	...	4	4½	42	16¾
4. J. S.	...	5	...	48	19
5. M. A.	...	4	8½	47	18½
6. D. A.	...	4	3	43	17
7. L. F.	...	4	13	45.5	18
8. T. R. M.	...	4	13	47	18½
9. N. B.	...	4	1	47	18½
10. P.	...	4	10	47	18½
11. C. S.	...	3	11	44.25	17½
12. M. V.	...	4	3	48	19
13. B.	6	2	12	38	15
14. P.	7	2	2½	36	14¼
15. S. C.	...	4	2	43	16¾
16. F. H.	...	2	13	37.5	14¾
17. M. V.	6	1	12	33.5	13¼
18. E.	7	2	5½	35	14
19. C.	7	2	15½	38.5	15⅛
20. A. U.	...	2	5½	35	14
21. No. 767	...	2	13	..	16½
22. No. 766	...	3	4	30 (?)	....
23. No. 263	...	2	16	34	....

At Bellevue Hospital, because of the prospect of entirely new children's wards, a very simple and inexpensive premature ward was devised for temporary use. The sunny corner of a ward facing southwest was partitioned off and double windows with transoms were installed and the number of radiators was increased, so as to furnish

sufficient heat on the coldest days. Ventilation was secured by means of the transoms and the door leading into the rest of the ward, where three wet nurses and their babies have their beds. The premature room has a capacity of ten cribs, with a cubic air space of 1,000 feet per crib. Moisture for the air is obtained by keeping a large pan of water simmering on an electric stove. After much experimenting we found that the babies do best, as a rule, when the temperature is kept from 76 to 80 F. with a humidity between 60 and 70 per cent. Without this degree of moisture the room temperature had to be much higher, and even then the babies' mouths got very dry, and their appetites and digestion did not seem so good. Very feeble infants are not only wrapped in cotton, but hot water bottles are put at the bottom and sides of the crib until the baby gains enough strength to keep an even temperature without them. Few need the bottles for more than a week.

Incidentally, we have found the warm ward of the greatest advantage in managing feeble infants that are not premature, such as those weighing 6 pounds at 6 months and having a subnormal temperature. On being put into the warm ward the temperature comes up to normal and they soon begin to assimilate and utilize the same food which seemed to be of little use when their temperature was subnormal.

The baby should be handled only when absolutely necessary. For the first few days after the initial anointing with oil there should be no undressing of the baby, the only handling being that necessary to change the gauze diaper. The clothing should be the simplest possible. Babies under 4 pounds are best wrapped in cotton and kept so swathed until the temperature remains constantly at normal and the weight has risen to 4 or 4½ pounds.

After the initial sponge bath and oiling no bath needs to be given for 4 or 5 days; then a sponge bath may be given every other day for a few days, and later every day.

Diet and Method of Administration.—Of equal importance with the maintenance of body heat is the diet and its administration. In order, then, to feed these babies we must put the food into their mouths and often even into the stomach. In general, the most satisfactory means of administering the food is to use a Breck feeder. This is a large graduated tube with a rubber bulb at one end and a small nipple at the other. After the warm food is put into the tube, the nipple is inserted into the baby's mouth, the bulb adjusted and then slight pressure will express a small amount of food through the

nipple into the baby's mouth. This has the advantage of teaching the baby to draw on the nipple, but without exhausting the baby's strength. Feeding by the medicine dropper is not nearly so satisfactory, because it does not teach the baby the proper movements of the tongue and

TABLE 3.—Data of Infants Cured

First Weight, Lb.	Oz.	Length, Cm.	Discharge Weight, Lb.	Oz.	Time in Hospital, Mo.	Food
4	6	33	5	1	3	At first took breast milk ¾, barley water ¼. Later 6% 5 in 20 with 1 ounce dextrimaltose
3	..	43	5	5	4	First food breast milk and whey ⅔ to ¾ strength. Later in conjunction with or entirely 6% 5 in 20, with 1 ounce dextrimaltose
4	2	..	6	6	4	Breast milk gradually changed to top milk modification
2	13½	..	5	6½	7	One-half strength breast milk alternated with 6% 5 in 20. Later whole milk 7, dextrimaltose 1½, barley water to 24½, with the addition of ½ yolk of egg twice daily. 3¼ ounces, 7 feedings
4	10	..	5	4	1¼	Breast milk gradually changed to top milk modification
3	14	..	5	1	3½	Breast milk and whey, gradually changed to alternation with modified milk; calories 80 to 160. Did best on 140 calories
3	15	..	4	14	1½	Calories 100 to 150
3	14	..	6	2	2½	Breast milk gradually changed to top milk modification
3	13	..	4	11	1½	Baby had bronchopneumonia with temperature up to 104; did best on about 170 calories; took no breast milk; had either modified 6% milk or modified whole milk
4	5	..	4	6½	After 1 week	Breast milk gradually changed to top milk modification
4	..	..	5	13½	2	At first 6% milk 3½, milk sugar ¾ and barley water to 16, 2, 8 feedings, 119 calories. Next 6% milk 4½, 2 ounces, 8 feedings, 160 calories. Gained on this to 4 pounds 10½ ounces. Next 7% milk 5 ounces, milk sugar ¾ to 1, barley water up to 20, 125 calories. Gained on this to 5 pounds 4 ounces
4	2	..	5	1	2	Breast milk gradually changed to top milk modification
4	12	.	5	9	¾	7% milk 5, dextrimaltose 1, Granum water to 20, 2½ ounces, 8 feedings, or 125 calories. Food never changed
3	11	..	4	15	2	Never took any breast milk, but 6% 5 in 20 with dextrimaltose 1 ounce, quantity being increased from 1 to 2 ounces, 8 feedings

lips, and because, also, it is a much slower method of administering food. In some cases the baby cannot swallow satisfactorily and then it is necessary to resort to gavage, a very small, soft rubber catheter being passed through the mouth or through the nose. It is found that the baby is less apt to vomit when it is passed through the nose.

The food which is most suitable and requires the least digestive effort on the part of the baby is, of course, breast milk, but even this must usually be diluted and perhaps even predigested. At Bellevue three wet nurses are kept constantly to furnish milk for the premature babies, and often additional breast milk is bought from women in the neighborhood. This is a good charity for both the women and for the hospital baby. In all private cases the effort should be made to secure good breast milk, either obtained from some maternity hospital or better from a wet nurse who is in the house along with her own baby. This last is necessary in order to keep the breast milk from drying up. The milk is to be expressed from the breast two or three times a day and a requisite quantity mixed with either whey, barley water or granum water as a diluent and then fed to the baby from a Breck feeder. The mixture of breast milk which we generally employ in our premature wards in Bellevue Hospital is for the first few days one half whey and one half breast milk, 1 ounce being given every one and one half or two and one half hours, depending on the size of the baby and its stomach capacity. After a few days the strength of the breast milk is increased to three fourths, from 1 ounce to 1½ ounces being given seven or eight times in twenty-four hours. We have had no success with the four-hour interval. On this food the babies will usually gain quite satisfactorily, though at first very slowly, and one should not be discouraged if the increase in weight is not more than 1½ or 2 ounces per week. So long as the baby is comfortable and has a normal temperature one should be quite satisfied with such a gain. Later the breast milk can be increased to full strength and the quantity given in twenty-four hours also increased, so that the baby will be taking 2 ounces every three hours. This should be sufficient food for a baby weighing 4½ or 5 pounds. If it is impossible to obtain breast milk one must then make use of some cow's milk modification. We have found it most satisfactory to use 6 per cent. top milk as the basis of the modification and to dilute this at first with whey or with a gruel made from Imperial Granum; often both the whey and the granum are used as a diluent. Five ounces of 6 per cent. milk, 10 ounces of whey and 5 ounces Imperial Granum water are used to make up a 20-ounce mixture. To this is added either milk sugar or more often dextrimaltose in quantity from ½ ounce to 1½ ounces.

If the baby is very feeble, the food is always boiled to prevent the formation of firm casein curds, and also predigested with a pancreatic

extract for the purpose not only of peptonizing, but also for the purpose of emulsifying the fat and converting into maltose part of the dextrin and starch in the diluent. Occasionally we have made use of potassium carbonate, 3 or 4 grains to the day's feeding, as an alkali to prevent any chance of acidosis, and occasionally also we have made use of sodium citrate, with the idea of hurrying the food through the stomach into the intestines.

The number of calories per kilogram required by premature babies is, as would be expected, much higher than for babies at full term. We have found by experience that giving the usual 100 calories per kilogram seldom results in a satisfactory gain. On the contrary, on account of the greater proportional surface area it is usually necessary to increase the number of calories from 1¼ to 1½ times the ordinary requirements. In looking through the charts it is found that most of these premature babies do not gain until the calories per kilogram have reached at least 120 and many times as high as 150 or more per kilogram. As the baby increases in weight and its subcutaneous fat increases, the caloric requirement diminishes, so that by the time the weight of 5 pounds is reached the calories may generally be safely reduced to 110 or 120.

An important accessory apparatus in the premature room is a tank of oxygen all coupled up and ready for instant use in case of cyanotic attacks. It often proves life-saving.

Prognosis.—As to this, the period of uterogestation is of great importance, but not entirely conclusive. The weight is the best criterion, but we must not despair of even the very smallest babies. If the baby weighs under three pounds, the chances are very poor; every ounce over three pounds improves the prognosis. I have already mentioned cases of babies weighing 2 pounds 3 ounces and 2 pounds 13 ounces that gained most satisfactorily. Another baby on admission when 5 days old weighed 2 pounds 10 ounces, and at the age of 1½ months had gained only 1 ounce, weighing 2 pounds 11 ounces. It became a very strong, vigorous infant weighing 4 pounds 13 ounces and was graduated from the hospital at the weight of 5 pounds. It must be remarked here that if the baby is over one week old, although very small, it has a much better chance to live, no matter what the weight. The very fact of having survived a week with so small a body augers a very good constitution, and with proper care there is every likelihood that the baby can survive.

CASE REPORTS

Baby J. L. weighed at 10 days 2 pounds 3 ounces, 7 months' gestation, and was 43 cm. long. At first fed on breast milk one-half strength; later three-fourths breast milk and one-fourth whey, 177 calories, when eight feedings of 1½ ounces were given. It gained well on this to 3 pounds 14 ounces. It then lost 1 ounce; then the food was peptonized and potassium citrate added. It gained to 3 pounds 1 ounce, when it was put on whole milk 7 in 20 with 1 ounce dextrimaltose, seven feedings of 2½ ounces. On this the baby gained up to 4 pounds 13½ ounces. Then it suffered gonococcous infection and had to be removed from the premature ward for isolation. The infection and the less expert care caused the baby to lose rapidly and it died, weighing 4 pounds 4 ounces.

DISCUSSION

Dr. Veeder: We have a room in the Children's Hospital in St. Louis similar to the one described by Dr. La Fétra. Our experience, however, has been somewhat different. We have wasted considerable money in trying to get a system of control for this room, and have been unsuccessful. We now open the transom over the top of the window and heat the room by means of radiators, having the nurses watch the temperature carefully. We keep the temperature at 85 F., and do not dress the child except in ordinary infant clothing, leaving it absolutely uncovered on the bed and we do not put it in cotton. We have noted that a great many children will not gain until they have a higher caloric value of the food. At times not 125 calories, but from 170 to 185 calories, seem necessary. The curve of gain is interesting. The babies gain only an ounce or so a week for a month or six weeks, and then begin to gain rapidly on the same food as before. After they have been in the warm room for about two months, the curve flattens out again, and another increase in weight cannot be obtained until the baby is taken from the warm room and placed in the ordinary ward. Then the weight goes up again.

Dr. Sedgwick: Dr. La Fétra has made a statement that I think I shall have to defend for my friend, Dr. J. C. Litzenberg of Minneapolis, who reported, in the section on diseases of children at the Atlantic City meeting of the American Medical Association in 1912, on the four-hour feeding of premature infants. I think that was the first report on the subject made in this country. Since then the newborn work has been transferred from obstetrics to pediatrics in teaching institutions, and we have had charge of the work. We have had success with the four-hour feedings of premature infants. Dr. La Fétra says that he has not. These infants are all well and blooming, and they are doing the same in other parts of the country. Last year Dr. Howland, who is not here, said, "We are doing it now, and it works"; so others get results with the four-hour interval. Of course, we have sometimes to use gavage. It can be done and it has many points in its favor.

Dr. La Fétra: In view of the fact that I made a point of our not having succeeded, I should like to have Dr. Sedgwick tell us the technic of the four-hour feeding. I shall be glad to make another trial. Dr. Hoobler and I made a trial in my wards, but we did not succeed in getting enough food into the baby in twenty-four hours by the four-hour feedings.

Dr. Sedgwick: We put in more than the ordinary chart of the stomach contents of premature infants would indicate as possible, for we know that the stomach contents of the infants move on, as we put the infants under the

fluoroscope. The amount the child can take does not depend entirely on the anatomy of the stomach. We can get a sufficient number of calories in. We run from 120 to 150, and we have no trouble in getting more in, if necessary.

A point that Dr. Litzenberg brought out particularly was the fact that we have so little vomiting. We always feed these babies now by tube. It is easier for the baby and easier for the nurse. The baby rests better. We can put more milk in and get the calories wherever we want them.

Dr. La Fétra: How much do you put in, and what?

Dr. Sedgwick: We always use breast milk, and put in enough to raise the calories to between 120 and 150. Did I answer your question?

Dr. La Fétra: Not exactly. How many ounces or cubic centimeters do you give?

Dr. Sedgwick: We have no rule in regard to that. We usually start with 10 or 15 c.c. five times a day, and raise it as rapidly as possible up to the amount necessary. We have no rule in regard to giving so much at a time. We put in a small amount at first and raise it as rapidly as possible, noting the results in the child.

Dr. Hoobler: I want to speak of the possibility of transferring what has been done in Bellevue Hospital into any home. Is it possible to provide this in a well-ordered home? I tried this out this winter, during very severe weather, with a 4-pound premature child. We were able to maintain the room temperature at the point which Dr. La Fétra has described as being the most satisfactory, with the humidity in proper proportion.

One additional thing we tried, and we believe it excellent for keeping the baby warm. We took a clothes basket and with barrel hoops made a little tent, covering it with a blanket. Under the blanket we hung a couple of ground-glass electric bulbs, and between these bulbs and the baby's face we hung a large piece of black cloth. We hung a thermometer within the tent, and we could regulate the temperature of the tent perfectly. We tried to keep the room temperature around 75 F., but in very severe weather this was sometimes difficult. We could, however, keep the temperature of the tent up to as high as 90 F., regardless of outdoor conditions. Keeping the baby under these favorable conditions seemed to assist greatly its nutrition.

FURTHER EXPERIENCE WITH HOMOGENIZED OLIVE OIL MIXTURES

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In February, 1915, before the New England Pediatric Society, and in May, 1915, before the American Pediatric Society, I called attention to the possible uses of the homogenizing machine of M. Gaulin of Paris, for purposes of modifying milk for difficult cases of feeding, especially those showing intolerance for fat.

Briefly stated, homogenization of liquids of different densities consists in reducing the constituent elements to such a physical condition that they will no longer separate but will maintain a permanent and even composition throughout the mixture. This object is attained by means of a powerful pump, which forces the mixture through a finely ground agate valve against a pressure of from 3,000 to 5,000 pounds to the square inch. In the case of mixture of milk and oils, the fat globules are so crushed and pulverized that they became incorporated with the other elements of the milk so that they no longer rise by action of gravity or separate after long standing. It is possible by this process to improve the emulsion of a modification of cow's milk so that it will be even finer than that of breast milk, without altering in any way the chemical properties of the milk. There is reason to believe that a milk so treated may be better digested and assimilated. Still more interesting, however, is the possibility of substituting some other fat than cow's fat in cases of malnutrition, in which it is often difficult to give enough fat to make a child gain normally in weight without precipitating sooner or later a digestive crisis.

These cases of difficult feeding respond best of all to breast milk, which contains anywhere from two to three times as much fat as the child will take in cow's milk modification. It is a question, therefore, whether such cases are correctly classified as due to fat intolerance. It would appear more reasonable to suppose the so-called intolerance to be due to something which is peculiar to cow's fat and is not present in breast milk.

The principal differences in the fats of cow's milk and human milk are the size of the fat globules and the proportion of volatile fatty acids. The proportion of volatile fatty acids in breast milk is 2.5 per cent. of the total fat; in cow's milk 27 per cent. of the total fat. The nonvolatile fats are made up mostly of olein and palmitin in both cow's milk and breast milk. Olive oil is almost wholly olein and palmitin, and free from the volatile fatty acids which form such a large proportion of cow's milk fat. It was my suggestion, therefore, to utilize olive oil to obtain the fat percentages in modified milk mixtures and so to eliminate the volatile fatty acids; and also by homogenization to secure an emulsion as fine as or finer than that of human milk. The milk sugar and proteins were to be obtained from skimmed milk as usual, and additional carbohydrates, in the form of dextrin-maltose and starch prescribed according to the usual indications.

This method of feeding has been applied to thirty-seven cases, of which twelve occurred in private practice and twenty-five in the outpatient department of the Children's Hospital. The present series includes the subsequent histories of the cases reported last year. I have not included in this list the older children, whose diet was from the start a mixed one, and which would, therefore, come into another class. I have also excluded one private case of congenital heart and enlarged thymus, two or three hospital children who had the milk for a few days only, and a few who have recently been started. The series as tabulated includes practically all of the cases of difficult feeding that I have had an opportunity to study.

It should be borne in mind that the hospital cases which I used were cases of babies who had been under treatment for malnutrition and indigestion for considerable periods without making satisfactory progress in their weight development under the usual methods of feeding. The average length of this period of outpatient feeding in this series, before beginning the homogenized olive oil mixtures, was three months. The result of previous feedings is best appreciated when one understands that the average number of months was 6.3 with an average gain of only 5 ounces per month. Naturally, in such a series all types and degrees of indigestion were met with. It is not difficult to modify milk in such a way that fairly normal movements and freedom from discomfort are obtained, but the failure of the feeding is shown by the lack of normal weight development, and by digestive disturb-

ances brought about when the attempt is made to raise the fats to such a point that normal gains in weight should be expected.

A normal, healthy baby gains, according to a high standard of growth, 14 pounds in twelve months, or an average of 18.7 ounces per month.

In my series of thirty-seven patients, whose average gain on previous feedings was 5 ounces per month, for a period of 6.3 months, the average gain per month was 18.15 ounces, or within ½ ounce per month of the normal, healthy infant. This represents a gain of three and one-half times (363 per cent.) over that of the previous feeding. The average period of the homogenized olive oil feeding was 4.7 months, a sufficient time to determine its permanent effects.

The improvement in the babies' general condition has been as striking as that of their gain in weight. Vomiting and sour regurgitation, when present as symptoms, are quickly relieved. The child improves in strength, in the quality of its fat and in the development of its functions, as one expects it to improve in normal, successful feeding. The appetite improves rapidly, and the stools soon become normal in appearance, if the sugars are intelligently prescribed. By this I refer to proper proportions of dextrin and maltose. When there is a tendency to looseness, I have used the preparation known as "dextri-maltose," for the extra carbohydrates; on the other hand, when the bowels are constipated, the usual laboratory "maltose," or malt soup preparations, are preferable. In many cases a combination of the two will bring about a normal stool if used in proportions suited to the individual child. Barley water (0.75 per cent.) was used in nearly every case. In some cases the mixture was heated to 212 F., in others given unheated. Lime water was usually given in amounts of from 5 to 10 per cent. of the total mixture, but not as a matter of routine.

The percentage of olive oil was almost invariably started at 1.5 and did not exceed 3.5 per cent. The indication for raising this was the rate of gain and sense of hunger. The total carbohydrate was usually started at about 5 per cent. and never exceeded 7 per cent. The proteins were started at 1.5 per cent. and seldom exceeded 2 per cent. In my opinion, hunger is the safest guide as to the child's tolerance for the amount of fat it is taking. If the appetite remains keen, the olive oil is being well taken care of; if too much fat appears in the stools or if diarrhea and vomiting occur, a loss of appetite almost invariably occurs and gives positive indication for a reduction of both

fats and sugars. According to Freund the average normal proportion of soaps in the stools is 18.3 per cent. of the total fat, the extreme limits varying from 4.9 per cent. to 35.9 per cent. The mere presence of soaps in the stools, therefore, unless quantitatively determined to be beyond the normal limit, is not of itself a sure indication of fat intolerance.

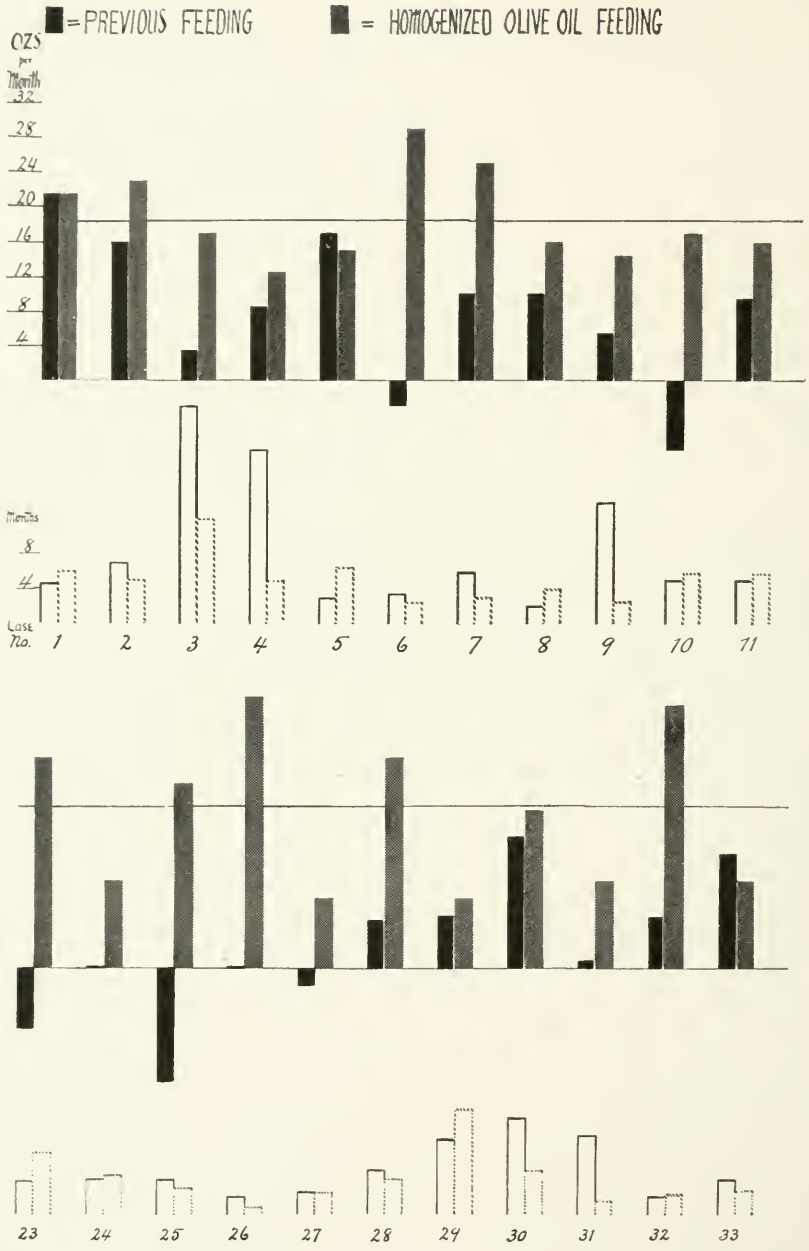
This method of dealing with cases of fat intolerance and other cases of difficult feeding is applicable in cities supplied by milk laboratories and in hospitals which will incur the expense of installing a homogenizing machine. If further experience in a larger number of cases is in line with the results I have obtained in a comparatively small series, such an expense will be fully justified.

OLIVE OIL MIXTURES IN INFECTIOUS DIARRHEAS

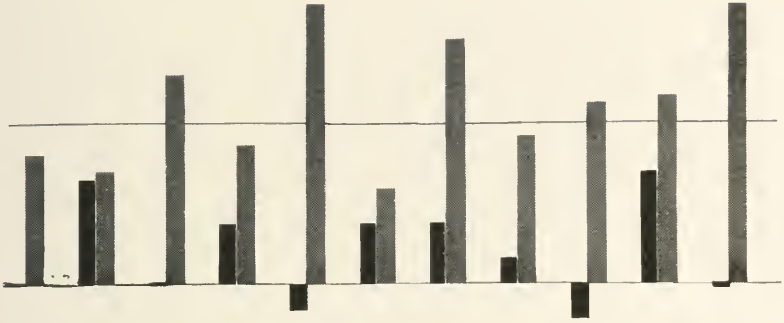
As my experience during the winter had convinced me that olive oil homogenized in milk mixtures was well tolerated in the diarrheas due to indigestion and fermentation, I was interested to see if it could not be safely used in the early days of convalescence from infectious diarrheas to supply additional calories and prevent or lessen the loss of weight which occurs in such cases.

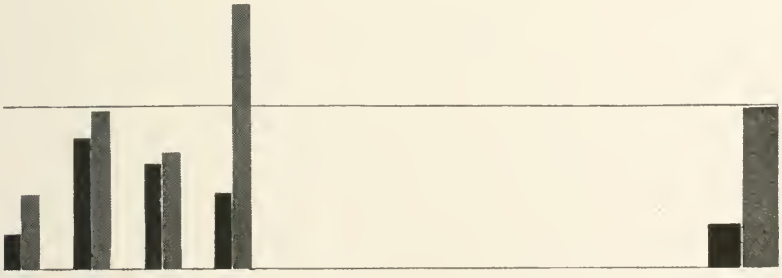
Owing to the courtesy of Dr. Bowditch, Dr. Wyman made use of this suggestion last summer in his service at the Floating Hospital. The general scheme of treatment was as follows: After the initial period of cartharsis and starvation, a fat-free lactic acid milk, diluted two thirds or one half, was given. If the infecting organism proved to be of the Flexner or Shiga type, dextri-maltose was added up to 4 or 5 per cent. and sometimes barley water. If the gas bacillus was present, no carbohydrates were added. After a period of several days, when the acute febrile disturbance showed distinct signs of subsiding, olive oil was homogenized with the lactic acid milk, in percentages of from 1 to 1.5, and if well tolerated 2, thus adding considerably to the caloric value of the blood.

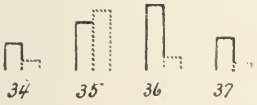
The results briefly summarized were as follows: There were nineteen cases of infectious diarrhea on the service, fifteen of Flexner bacillus type, one of the gas bacillus, and three undetermined. Four patients died, giving a mortality of 22 per cent., about the same, I am informed, as in the other services. Of the fifteen patients who lived, eight were in the hospital on an average of twenty-one days each and lost over their entrance weight an average of 15 ounces.



In an attempt to express the results of these feeding cases in a form which will be readily understood, I have in the chart reduced the total gain to the average number of ounces gained per month, during the previous feedings (on the left) and during the homogenized olive oil feedings (on the right) for each case. The upper horizontal black line represents the average number







of ounces per month gained by the normal healthy infant. The relative gain in both periods of feeding is at once apparent, and a comparison is readily made with that of a normal infant. Below, on the left, are charted the number of months the infants were on the previous feeding; and on the right the number of months they were on the homogenized olive oil milk in each case.

Seven were in the hospital on an average of fourteen days each, and gained an average of 10.7 ounces over their entrance weight. The average net loss of all fifteen surviving patients was therefore only 3 ounces over their entrance weight.. Whether this showing was better or worse than in the other services we have no statistics to show. It is my opinion, however, based on this limited series of cases, that olive oil homogenized can be given safely after the severe acute febrile stage has passed and in the period of convalescence and is more effective in making up the loss of weight than the fat of cow's milk.

FAT METABOLISM OF INFANTS FED ON HOMOGENIZED MILK

A study of the fat metabolism of infants fed on homogenized olive oil, homogenized whole milk and ordinary cream mixtures was carried out on the Boston Floating Hospital during 1915 season, by Dr. C. H. Laws of the University of Michigan, under the chief chemist, Dr. Bosworth. Through the courtesy of Dr. W. R. Bloor, Dr. Laws was allowed the use of the laboratory in the Biochemical Department of Harvard University Medical School. The detailed results of these experiments will be included in a subsequent paper.

There were three observation periods (two in Case 4), each of six or seven consecutive days, with an interval of from four to eight days of rest off the frames.

In these experiments the relative degrees of fat absorption in the three types of mixtures used were as follows:

Case 1. Homogenized whole milk—whole milk—homogenized olive oil.

Case 2. Homogenized olive oil—whole milk—homogenized whole milk.

Case 3. Homogenized whole milk—whole milk—homogenized olive oil.

Case 4. Whole milk—homogenized olive oil.

Objection may reasonably be made to any definite conclusions drawn from the above results, owing to (1) possible limit of error in the method of fat estimation, and to the fact that the differences in fat absorption was not sufficiently marked to be conclusive; (2) failure to estimate daily the fat percentage of the food, and the assumption that the formula was actually as calculated; (3) the artificial conditions to which the babies were subjected while confined to the frames;

and (4) inevitable variations in individual conditions, which might alter decidedly the significance of the determinations.

The result of the clinical cases extending over a period of nearly five months on an average are, however, of decided significance and justify the belief that homogenization of milk mixtures and the substitution of olive oil for cow's fat offers an additional and valuable resource in infant feeding in cases of difficult digestion with malnutrition. The efficiency of such mixtures would appear to be due either to the quality of the olive oil fat, or to the absence of certain harmful ingredients of cow's fat. The process of homogenization is merely a means of mechanically subdividing the fat so that it may be efficiently utilized in the processes of digestion.

EXPLANATORY NOTES ON FEEDING CHARTS

No. 1.—Rueter—A normal feeding case. Cow's milk modification throughout; homogenized in the second period, showing approximately the same rate of gain in the second half year as in the first six months.

No. 2.—Bartlett—A normal feeding case, cow's milk throughout, homogenized in the second period with increased rate of gain.

No. 3.—Dutch—Previous feeding, twenty-five months, with average gain of 3½ ounces per month. Homogenized cow's milk mixtures tried with no gain in weight. Homogenized olive oil mixtures for twelve months, with an average of 17 ounces per month.

No. 4.—Forbes—Previous feeding of twenty months with average gain of 8.6 ounces per month. Homogenized olive oil for five months, with average gain of 12.5 ounces per month, during which time child had measles and pertussis.

No. 5.—Watts—Pylorospasm—Previous feeding three months, with average gain of 17 ounces per month. Homogenized olive oil for six and one-half months, with average gain of 15 ounces per month, during which time the baby had one attack of bronchopneumonia and two attacks of influenza with bronchitis.

No. 6.—Hanly—Pylorospasm—severe Previous feeding three and one-half months with an average loss of 3 ounces per month. Homogenized olive oil two and one-half months with the average gain of 29 ounces per month. Vomiting finally stopped.

No. 7.—Kelley—Pylorospasm—Previous feeding six months, average gain of 10 ounces per month. Homogenized olive oil three months, with average gain of 25 ounces per month. Vomiting finally stopped.

No. 8.—Channing—Pyolorospasm—Previous feeding, two months, with average gain of 10 ounces per month. Homogenized olive oil, four months with average gain of 16 ounces per month. Vomiting stopped.

No. 9.—MacDonald—Pylorospasm—Previous feeding fourteen months, with average gain of 6.5 ounces per month. Homogenized olive oil two and one-half months, with average gain of 14.4 ounces per month.

No. 10.—Russell—Pylorospasm—Operation. Breast-fed. Vomiting continued. Five months, lost an average of 8 ounces per month. Homogenized olive oil five and three-quarters months, with average gain of 17 ounces per month. Vomiting finally stopped. For six weeks tried modified cow's milk. Vomiting, fatty stools and stationary weight recurred. Resumed olive oil milk and child gained 42 ounces in forty-seven days.

No. 11.—Nelson—Previous feeding five months, with average gain of 9½ ounces per month. Homogenized olive oil three and three-quarters months, with average gain of 16 ounces per month.

No. 12.—Davis—Previous feeding four months, with no gain. Homogenized olive oil six months, with an average gain of 15 ounces per month.

No. 13.—Tower—Previous feeding six months, with an average gain of 12 ounces per month. Homogenized olive oil five and three-quarters months, including convalescence from severe infectious diarrhea, with average gain of 13 ounces per month.

No. 14.—Di Pietro—Previous feeding six months, with no gain. Discharged from hospital unrelieved with diagnosis of fat intolerance. Homogenized olive oil eight and two-thirds months, with an average gain of 24 ounces per month.

No. 15.—Kennedy—Previous feeding five and one-half months, with an average gain of 7 ounces per month. Homogenized olive oil six and three-quarters months, with an average gain of 16 ounces per month.

No. 16.—Keough—Previous feeding six months, with an average loss of 3 ounces per month. Homogenized olive oil for two and three-quarters months, with an average gain of 32 ounces per month.

No. 17.—Shaw—Previous feeding six and one-half months, with an average gain of 7 ounces per month. Homogenized olive oil three

and three-quarters months, with an average gain of 11 ounces per month.

No. 18.—Sullivan—Previous feeding eight months, with an average gain of 7 ounces per month. Homogenized olive oil six and one-half months, with an average gain of 28 ounces per month.

No. 19.—Maguire—Previous feeding twelve months, with an average gain of 6 ounces per month. Homogenized olive oil two months, with an average gain of 17 ounces per month.

No. 20.—Alford—Previous feeding three months, mixed breast and bottle, average loss of 8 ounces per month. Homogenized olive oil seven months, with an average gain of 21½ ounces per month.

No. 21.—Di Natalie—Previous feeding two months, with an average gain of 13 ounces per month. Homogenized olive oil one and one-quarter months, with an average gain of 21½ ounces per month.

No. 22.—Giles—Previous feeding five months, with an average loss of 4 ounces per month. Homogenized olive oil two and one-third months, with an average gain of 32 ounces per month.

No. 23.—Sheehan—Previous feeding three and three-quarters months, with an average loss of 7 ounces per month. A distinct case of fat intolerance. Homogenized olive oil seven months, with an average gain of 24 ounces per month.

No. 24.—Doran—Previous feeding four months with no gain. Homogenized olive oil four and one-half months, with an average gain of 10 ounces per month. Child died suddenly of unknown cause.

No. 25.—Maddox—Previous feeding four months, with an average loss of 13 ounces per month. Homogenized olive oil three months, with an average gain of 21 ounces per month.

No. 26.—Magill—Previous feeding two months, with no gain. Sent to the hospital for pyloric stenosis. Homogenized olive oil one month, with a gain of 31 ounces.

No. 27.—Meroth—Previous feeding two and one-half months, with an average loss of 2 ounces per month. Homogenized olive oil two and one-half months, with an average gain of 8 ounces per month.

No. 28.—McKenzie—Previous feeding five months, with an average gain of 5½ ounces per month. Homogenized olive oil four months, with an average gain of 24 ounces per month.

No. 29.—Nichols—Previous feeding eight and one-half months, with an average gain of 6 ounces per month. Homogenized olive oil

twelve months, with an average gain of 8 ounces per month. Persistent vomiting immediately relieved. Progress slow, but final result good, with child on general infant diet.

No. 30.—Olsen—Previous feeding eleven months, average gain of 15 ounces per month. Homogenized olive oil five months, with average gain of 18 ounces per month.

No. 31.—Pistolozzi—Previous feeding nine months, with a gain of 1 ounce per month. Homogenized olive oil one and one-half months, with an average gain of 10 ounces per month, when the child developed pneumonia.

No. 32.—Gershonowitz—Previous feeding two months, average gain 6 ounces per month. Homogenized olive oil two and one-quarter months, with an average gain of 30 ounces per month.

No. 33.—Williams—Previous feeding four months, average gain per month 13 ounces. Homogenized olive oil two and three-quarters months, during which the baby had a green-stick fracture, acute otitis media and measles, average gain 10 ounces per month.

No. 34.—Roachford—A case of congenital syphilis. Previous feeding three months, average gain 4 ounces per month. Homogenized olive oil one month, gain 8½ ounces.

No. 35.—Barry—Previous feeding five and one-half months, average gain 15 ounces per month. Homogenized olive oil six and three-quarters months, average gain 18 ounces per month.

No. 36.—Mulvee—Previous feeding seven and one-half months, with an average gain of 12 ounces per month. Hemogenized olive oil one and one-half months, with an average gain of 13½ ounces per month.

No. 37.—Klibanoff—Previous feeding on breast milk three and three-quarters months, average gain of 8⅔ ounces per month. Homogenized olive oil two weeks, gained at the rate of 30 ounces per month. (Subsequent gain in the last six weeks at the same rate.)

270 Clarendon Street.

DISCUSSION

DR. LADD: I mentioned in my paper, I think, the fact that of the patients with infectious diarrhea that were fed in this way, four died, giving about the same percentage as in the other services. The method was not used until the period of convalescence. In infectious diarrhea it is a question of supplying a food that will be tolerated and on which the loss of weight which always occurs, will be most rapidly regained. Olive oil homogenized with fat-free lactic acid milk fulfilled these indications with satisfactory results.

DR. BOWDITCH: I am sorry that I have no figures to assist Dr. Ladd and the gentleman here from the other wards of the hospital, concerning convalescents from the use of homogenized olive oil mixtures. The children, however, do well. My own feeling is that the cases on the other side of the hospital, in two other wards, had the same mortality however, and did well there too; but I do not know what the difference was. Our experience last year was that after the initial treatment was established the children got well, who were going to get well, and that those who were not going to get well did not get well. Outside of that, I cannot offer anything.

STUDIES OF INFANT FEEDING

Sixth Paper

THE PREPARATION OF A SYNTHETIC MILK FOR USE IN STUDYING INFANT METABOLISM *

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INTRODUCTION

In connection with our investigations concerning infant feeding it became necessary for us to control all factors entering into the composition of the food used, and as only liquid foods can be used, it soon became evident that the preparation of a synthetic milk from pure materials offered the only solution of this problem. After many experiments, conducted during the past few years, we have finally perfected the method as given in this paper and have used synthetic milk prepared according to this method for several investigations with success. As many of our studies involve the use of synthetic milk we have decided to place the method on record for future reference.

The method in brief consists of four steps as follows:

1. The preparation of isolated food materials for use in making the synthetic milk.
2. The recombining of these materials to give a mixture of the desired composition.
3. The emulsification or homogenization of the fat and any of the solid or insoluble constituents entering into the composition of the food.
4. The pasteurization or sterilization of the food after it has been made.

We will take up each of these steps in detail.

PREPARATION OF MATERIALS

In making synthetic milk for our investigations some or all of the following substances may be used, as the case demands: Distilled water, pure fat, pure sugar, pure protein, pure salts of various kinds, the protein-free milk of Osborne and Mendel.

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* From the Biochemical Laboratory of The Boston Floating Hospital.

Fat.—So far, we have used only two fats, olive oil and butter fat. The olive oil used was the purest commercial oil we could obtain, but the butter fat has been a pure product prepared by us according to the method of Osborne and Mendel.

Sugar.—In some cases we have used the sugars of the purest commercial grade, while in others we have used recrystallized lactose.

Protein.—So far, we have used only one protein, casein, and have made use of this substance in three forms, the calcium caseinate of commerce (larosan), the sodium caseinate of commerce (nutrose) and pure casein or paracasein prepared according to the method already published by us in the *American Journal Diseases of Children.*

Salts.—The salts should all be of the highest purity and the ones most likely to be used will be the phosphates, chlorids, acetates and citrates of calcium, magnesium, sodium, potassium, etc.

Protein-Free Milk.—Osborne and Mendel have shown that a synthetic food made from pure materials contains none of the substances called vitamins which seem to be essential to promote the normal growth of an animal receiving such a food. These substances are present in a preparation made by them from milk and called protein-free milk. In investigations involving the continued use of a synthetic milk for more than a few days it is always wise, if the conditions of the experiment permit, to add some of this protein-free milk in order to obtain the benefit of the vitamins carried in it.

COMBINING THE INGREDIENTS

All our synthetic milks have been made up on the percentage basis, the amount of each constituent required being calculated and then weighed out into a clean beaker. The sugar is dissolved in one half the volume of distilled water required for the complete mixture and the salts added to this sugar solution. The protein is dissolved or suspended in the other half of the water. If larosan or nutrose are to be used they should be rubbed up to a fine paste with a small portion of the water, the remainder of the water carefully added and then the whole gently warmed in warm water to effect complete solution. Some difficulties will be encountered with these substances at first, but experience soon overcomes them. If pure casein or paracasein is used, it may be suspended in the water and homogenized with the fat or it may be dissolved by the addition of alkali, one half of a cubic centimeter of normal alkali or its equivalent being used for each gram of

protein. If strict percentages are to be observed, the volume of water used must be diminished by an amount equal to the volume of alkali solution used to dissolve the protein.

The two half volumes are now united, the fat melted and added, and the whole mixture homogenized.

HOMOGENIZING THE MIXTURE

The successful use of our synthetic milks for feeding investigations depends to a very great extent on our ability to produce a homogeneous mixture of considerable permanency and this result has been obtained by the use of a special homogenizing machine manufactured by the Manton-Gaulin Manufacturing Co. of Boston. This machine is a small one of special design built for laboratory use and is run by a small electric motor, the whole apparatus, motor, homogenizing chamber and pumps, being mounted on one base. A photograph of the complete apparatus is appended.

Before using the machine must be thoroughly washed in the following manner: All dust and grease is first removed by pumping a hot soap solution through the machine several times and the soap removed with hot water. A solution of hydrogen peroxid is now pumped through the apparatus for fifteen minutes and the last traces of this removed by the use of hot, recently boiled distilled water. The machine is now ready for use.

Mixtures containing liquid fats may be homogenized at once without warming, although much more satisfactory results will be obtained if the mixture is warmed slightly. Mixtures containing solid or semi-solid fats must be heated to a temperature a few degrees above the melting point of the fat used.

In transferring the mixture to the reservoir of the homogenizer it is well to allow all the fat to enter first with a small portion of the liquid, the fat and this liquid being allowed to run through the homogenizing chamber once or twice at a pressure of 50 kg. per square centimeter. This preliminary treatment breaks up the fat to a considerable degree and allows it to be mixed with the remainder of the mixture. The pressure is now increased to 150 kg. and the whole mixture run through the machine, after which the pressure is increased to from 200 to 250 kg. and the mixture run through the machine once or twice more.

In appearance the mixture now strongly resembles milk, the fat emulsion being quite permanent and the cream, which rises on prolonged standing, being easily shaken back into the mixture.

THE PASTEURIZATION OR STERILIZATION

The synthetic milk is now transferred to glass fruit-jars (lightning jars with glass tops are the best), the rubbers and tops put in place loosely and the jars placed in a large pan containing boiling water to a depth of about two thirds the height of the jars. The water is allowed to boil gently for thirty minutes, after which the covers are fastened and the jars are removed and allowed to cool. If the food is to be kept for any number of days it should be heated again in the same manner two days later and then stored in a cold place.

In our early experiments in the development of our synthetic milk we were allowed the use of the homogenizing apparatus in the Walker-Gordon Laboratory of Boston, and we take this opportunity to express our appreciation, especially to Mr. B. W. Nichols of that laboratory, who gave us much practical advice and assistance.

A STUDY OF THE TOPOGRAPHY OF THE PULMONARY FISSURES AND LOBES IN INFANTS

WITH SPECIAL REFERENCE TO THORACENTESIS *

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In the course of a general study of the anatomy of the infant's chest it seemed to us desirable to attempt to determine accurately the relation of the fissures of the lung to the bony framework of the thorax. We felt that carefully obtained data would be valuable not only for comparison with similar relations as they exist in the adult, but also as a stimulus toward greater accuracy in the clinical diagnosis of pleuropulmonary disease.

A careful search of the standard textbooks and of the periodical literature which has appeared since 1905 shows nothing in reference to the course of the fissures in infants. Symington[1] states that the only gross difference between the position of the lungs in children and in adults lies in the fact that in the former the anterior margins of the lungs are not as closely approximated as in the adult, in other words, that the right and left lungs at times do not meet or overlap under the manubrium sterni. He makes no mention of any difference in the course or relations of the fissures. On the other hand, there are numerous references pertaining to adults. Many of these doubtless are mere copied repetitions, but the conflicting descriptions point to the conclusion that the course of the interlobar fissures is fixed only within comparatively wide limits.

The right lung, it will be remembered, normally possesses two fissures. One of these, the oblique, starts above and behind and runs downward, outward and then forward; the second, the horizontal fissure, begins at a variable point above the middle of the oblique fissure and passes almost horizontally in toward the sternum.

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* From the Laboratory of Anatomy of the University of Pennsylvania.

1. Symington, J.: The Anatomy of the Child, E. & S. Livingstone, Edinburgh, 1887, p. 64.

The left lung normally possesses but a single fissure, the oblique, which corresponds to the like structure on the right side.

Various anomalous fissures exist quite frequently, the most common, according to Shaffner,[2] being found on the lower surface of the lower lobe. This is sometimes merely a shallow indentation, but at others is a deep fissure sharply delimiting the inner portion of the lower lobe.

In addition to anomalous fissures, there are also found at times variations in the normal fissures. Of the latter the horizontal is the one most frequently found to be atypical and at times it may be absent. Conversely, in the left lung, a transverse fissure occasionally is found dividing it into three lobes.

That the course of the oblique fissures in adults is far from constant may be inferred from the descriptions found in the literature.

Right Lung: It begins at the second dorsal vertebra (Morris,[3] Gray,[4] Deaver[5]), the second or third (Spalteholtz[6]), the third (Fraenkel[7]), the third or fourth (Corning[8]), the fourth (Bickham,[9] McClellan,[10] Davis,[11] Chauffard[12]), the fourth interspace or the fifth rib (Rochard[13]), the fifth rib or the fourth or fifth interspace (Piersol[14]). It terminates at the fifth intercostal space or the sixth rib

2. Shaffner, quoted by Piersol, George A.: Human Anatomy, J. B. Lippincott Co., Philadelphia, 1907, p. 1846.

3. Morris, Sir Henry: Human Anatomy, edited by J. P. McMurrich, P. Blakiston's Sons & Co., Philadelphia, 1907, Part 5, p. 1295.

4. Gray, Henry: Human Anatomy, edited by Robert Howden, Lea & Febiger, Philadelphia and New York, 1913, p. 1299.

5. Deaver, John B.: Surgical Anatomy, P. Blakiston's Son & Co., Philadelphia, 1903, iii, 409.

6. Spalteholtz, quoted by Dietlen, H.: Ergebn. d. inn. Med. u. Kinderh., 1913, xii, 197.

7. Fraenkel, A.: Therap. d. Gegenw., 1910, li, 337.

8. Corning, quoted by Dietlen, H.: Ergebn. d. inn. Med. u. Kinderh., 1913, xii, 197.

9. Bickham, Warren S.: Operative Surgery, W. B. Saunders Co., Philadelphia, 1908, p. 772.

10. McClellan, George: Regional Anatomy, J. B. Lippincott Co., Philadelphia, 1892, i, 267.

11. Davis, G. G.: Applied Anatomy, J. B. Lippincott Co., Philadelphia, 1913, p. 198.

12. Chauffard: Rev. gén. de clin. et de thérap., 1914, xxviii, 420.

13. Rochard, quoted by Gary, M. P.: Arch. de méd. et pharm. mil., 1910, lvi, 104.

14. Piersol, George A.: Human Anatomy, J. B. Lippincott Co., Philadelphia, 1907, p. 1859.

(Rochard,[13] Gray,[4] Davis,[11] Morris,[3] Deaver,[5] Piersol[14]), the seventh rib (Bickham,[9] McClellan,[10] Fraenkel[7]), the eighth rib (Chauffard[12]).

Left Lung: It begins at the second dorsal vertebra (Gray,[4] Morris,[3] Deaver[5]), the second or third dorsal vertebra (Spalteholtz[6]), the third rib (Bickham,[9] Fraenkel,[7] McClellan[10]), the third or fourth rib (Corning,[8] Davis[11]), the fourth interspace (Chauffard[12]), the third to the fifth rib (Piersol[14]). It terminates at the sixth rib according to

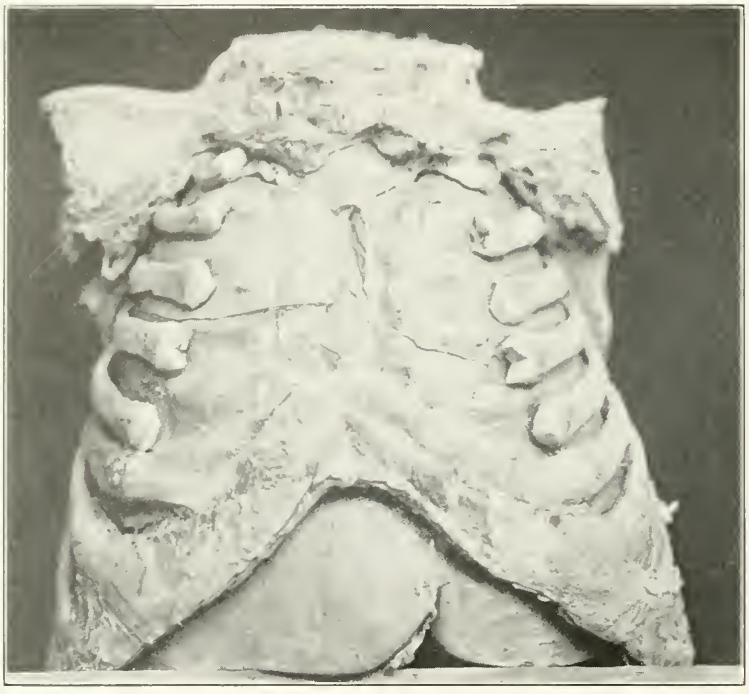

Fig. 1.—Photograph of a thorax showing the method of preparing the specimens for studying the relations of the pulmonary lobes and fissures in situ.

most of these authorities, except Chauffard,[12] who finds it at the seventh interspace.

Authors' Technic.—Our own observations are based on dissections of the formaldehyd-hardened bodies of fourteen infants, varying in age from 6 weeks to 15 months. Of these, six were under 4 months of age and six were 4 months or older; in two the exact age was unknown, but it approximated 3 to 6 months. In order to expose the

fissures in exact relation to the ribs, all of the soft tissues covering the ribs, sternum and spine, as well as the intercostal muscles and the parietal layer of the pleura, were carefully removed. Enough of the muscles of the shoulder girdle were left to insure stability of the clavicles, scapula and upper ribs. To allow of access to the interior of the chest the sternum was freed, the attachments of the costal cartilages being noticed in order to insure accurate replacement. The spine was allowed to remain untouched as a permanent support. As the bodies had been injected with formaldehyd, the manipulations essential to study in no wise disturbed the relationship of the structure as it had existed at the time of death. The photograph (Fig. 1) shows to a certain extent the result of one of the dissections, but it is impossible to depict in this manner the entire course of the fissures in relation to the ribs. By gentle separation of the ribs, however, this could accurately be determined in every case.

Unfortunately, the removal from our specimens of the soft tissues of the chest destroyed all the ordinary clinical landmarks of the axillary region. This is to be regretted, since the point of origin of the horizontal fissure from the oblique is a matter of considerable practical interest, mainly because it is the most obvious point of attack in dealing with a collection of pus between the upper and middle lobes.

An attempt was made to compensate for this loss of landmarks by marking the ribs with an indelible pencil or by nicking them with a knife before removing the pectoral and latissimus dorsi muscles. Neither of these methods was successful, as the pencil marks became smeared in the course of the subsequent dissection and the incisions into the ribs rendered them so fragile that the attempt was abandoned. In place of this we established the midpoint of the axilla by bisecting a horizontal line drawn from midsternum to the spinous process at a point just below the angle of the scapula. This we have called the midthoracic line.

In twenty-eight children in the wards of the Children's Hospital, varying in age from 15 days to 5 years, we compared the relation between this midthoracic line and the usual landmarks of the axilla, namely, the midaxillary and postaxillary lines. The latter landmarks were first located and carefully marked, and then the measurements for the midthoracic line were taken and compared with these markings. It was found that the midthoracic line invariably lay posterior to the midaxillary line, a distance varying from 0.5 to 2.5 cm. (average of all

cases, 1.27 cm.), while the postaxillary line lay posterior to the midthoracic line in every case but one, the distance varying from 0.5 to 1.5 cm. (average of all cases, 0.92 cm.). In the one exception, a child of 4 years, the midthoracic line lay 0.4 cm. posterior to the midaxillary line and exactly in the postaxillary line.

In general, we may say, therefore, that the midthoracic line lies approximately midway between the midaxillary and postaxillary lines. As the determination of the clinical landmarks by the eye is not so accurate or so reliable as the actual measurement by the tape, the latter procedure possesses distinct advantages.

Authors' Findings.—Our studies have shown us that the course of the pulmonary fissures in the infant may be described as follows:

Right Lung, Oblique Fissure: The origin is from the third to the fifth rib at the spine. In ten out of fourteen the point of origin was at the fourth rib or fourth interspace, in three at the third rib or third interspace and in one at the fifth rib, the average of fourteen cases being the fourth rib.

The course is downward and forward, crossing the midthoracic line between the third rib and the sixth interspace. Of the fourteen cases, one crossed at the third rib, two at the fourth rib, five at the fifth rib or fifth interspace and six at the sixth rib or sixth interspace, the average of fourteen cases being the fifth rib.

The termination is from the sixth to the seventh rib just posterior to the costochondral junction. Four were at the line of the costochondral junction and ten were from 1 to 3 cm. posterior to it. Of the fourteen cases, six terminated at the sixth rib, two at the sixth interspace and six at the seventh rib, the average of fourteen cases being the sixth interspace.

Right Lung, Transverse Fissure: The origin is from the third interspace to the sixth rib in the line of the oblique fissure. Of the fourteen cases, one was at the third interspace, seven were at the fourth rib or fourth interspace, five at the fifth rib or fifth interspace and one at the sixth rib, the average of fourteen cases being the fourth interspace.

The course is almost horizontal, either beneath the fourth rib or the interspace above or below it.

The termination is at the edge of the sternum from the third rib to the fourth interspace. Of the fourteen cases, six were at the third rib or third interspace, seven were at the fourth rib or fourth inter-

space and one was anomalous, terminating in the second interspace 3 cm. to the right of the sternal border, the average of thirteen cases being the upper border of the fourth rib.

Left Lung, Oblique Fissure: (In one case this fissure began at the fifth rib, passed downward more vertically than usual, crossing the midthoracic line at the eighth rib. Thence it continued forward beneath the eighth rib to its costochondral junction, an anomalous type. This is excluded from the summaries of this side, leaving but thirteen.)

The origin is from the second to the fifth rib. Of the thirteen cases, four were at the second rib or second interspace, two at the third rib or third interspace, seven at the fourth rib, the average of thirteen cases being the third interspace.

The course is downward and forward, crossing the midthoracic line behind the third to the sixth rib. Of the thirteen cases, one was at the third rib, four were at the fourth rib or fourth interspace, four at the fifth rib and four at the sixth rib. Average of thirteen cases, fifth rib.

The termination is from the sixth to the seventh rib at or posterior to the costochondral junction. Seven were at the line of the costochondral junction and the remainder about 1 cm. posterior to it. Of the thirteen cases, seven were at the sixth rib and six at the seventh rib, the average of thirteen cases being the sixth interspace.

To sum up, we find that the oblique fissure of the right lung in infants begins at the fourth rib (from the third to the fifth as extremes), crosses the midthoracic line between the fourth and sixth ribs and terminates between the sixth and seventh ribs, at or just posterior to the costochondral junction. In adults, according to the literature, the origin seems to be somewhat higher, although the tip of the dorsal vertebra, which is used as a landmark by some authors, almost corresponds to the rib below it, the second dorsal vertebra is equivalent to the third rib, etc. The point of termination seems to be the same in both infants and adults.

The oblique fissure of the left lung in infants begins at the third interspace (from the second to the fifth ribs as extremes), crosses the midthoracic line between the fourth and sixth ribs (as on the right side) and terminates between the sixth and seventh ribs, at or just posterior to the costochondral junction. In adults the origin and termination are described as being about the same as our findings in the infant.

The transverse fissure in infants begins at the line of the oblique fissure between the fourth and fifth ribs (from the third to the sixth rib as extremes) just in the midthoracic line or more often slightly posterior to it, and passes horizontally inward to terminate at the junction of the fourth rib or interspace and the sternum. In adults the exact beginning of the transverse fissure usually is not clearly described by the authorities consulted, but apparently it corresponds very closely to our findings in the infant.

It will be seen, therefore, that the differences between the fissures in adults and infants are slight and unimportant and that in both they show equally as marked variation in their point of origin, course and termination. Apparently this variability is dependent on no discoverable factors. We state this as the result of an attempt to establish some relationship between the anatomic characteristics of the chest and the location of the fissures. In this part of our study we investigated the following points in regard to the chest: (1) the general shape; (2) the anteroposterior and transverse diameters; (3) the circumference; (4) the subcostal angle; (5) the obliquity of the ribs, determined (a) at the spine and (b) in the midthoracic line. To these we added (6) the size of the liver (with special relation to the fissures of the right lung).

The result of this study was entirely fruitless and our conclusion is as stated above, namely, that these factors have no constant effect on the position of the fissures. We were somewhat surprised at this, as it would seem at first thought that the great difference between the shape of the chest in the adult and in the infant might readily influence the course and relationship of the fissures at the different ages. Apparently, however, the change in the shape of the chest goes pari passu with the development of the lung, with the result that the relation of fissure to rib or to interspace remains practically unchanged.

An important point is made by Dietlen,[15] who calls attention to the fact that descriptions of the course of the fissures refer only to the relations at the surface of the lung, since the planes formed by the inward projection of the fissures through the lung traverse various lines. This is of some importance in operations on interlobar collections, although the perfection of Roentgen-ray technic has rendered so much aid in determining localized collections of fluid as to minimize the importance of other aids to diagnosis. This is especially

15. Dietlen, Hans: Ergebn. d. inn. Med. u. Kinderh., 1913, xii, 197.

fortunate since the normal relations of the fissures are profoundly modified by interlobar collections.

We have been impressed with the fact that students and interns usually disregard the position of the fissures and fail to take advantage of the aid which may be gained from observing their relations. For example, an area of dulness involving the region of the right apex and sharply following the line of the horizontal fissure of the right lung usually will prove to be croupous pneumonia or its delayed resolution, rather than a tuberculous pneumonia. Again, an area of dulness which follows and lies below the line of the oblique fissure usually will be due to a pneumonia rather than to a collection of fluid in the pleural cavity, or a tuberculous pneumonia; while the gradual extension of the border of dulness beyond the limits of the lower half of the oblique fissure will point to an empyema, rather than to the extension of a pneumonic process, as the latter is more apt to involve another entire lobe or large section of a lobe.

An interlobar collection of pus, following a pneumonia of either the lower or the upper lobe, would be apt to show an irregular extension of the dulness at some point beyond the line of the oblique fissure, usually about the middle of its course, but differing in outline from that caused by the gradual formation of an empyema on the one hand or of a spreading pneumonia on the other.

In thoracentesis a matter of practical importance is the selection of the point for exploratory tapping of large collections of fluid in the pleural cavity. The object in such a procedure is to penetrate the chest wall at a point where the lung has been pushed away so far that it will not interfere with the suction in the exploratory needle. When tapping is done with the vacuum apparatus for the actual withdrawal of fluid, or when the surgeon is seeking to establish permanent drainage, the lowest point of the cavity consistent with safety evidently is the optimum point of attack. With reference chiefly to adults the choice of the majority of authors is the sixth, seventh or eighth interspace between the midaxillary and postaxillary lines. In tapping more or less localized collections the area of greatest dulness usually is selected, for obvious reasons. It were well, however, to confirm such choice by the evidence gained from stereoscopic plates and from the fluoroscope.

The lower part of the pleural sac (Fig. 2), that which lies between the chest wall and the diaphragm, is known as the costophrenic sinus,

or complemental space of Burns. It lies below the lower level of the lung during quiet respiration and extends as far down as the tenth rib in the midaxillary line (Piersol[14]). Its function is to afford space for the expansion caused by deep inspiration, but even with the most extreme effort, in an adult, it is doubtful whether the lung ever expands sufficiently to completely fill the space.

In infants and young children this costophrenic sinus is subject to even less expansion than it is in adults, owing to the less vigorous inspiratory excursions of the former. This applies with special force to the right side, where the relatively large size of the liver causes the diaphragm to rise more abruptly to its dome. During quiet respiration, therefore, the lower limits of the pulmonary lobes form the

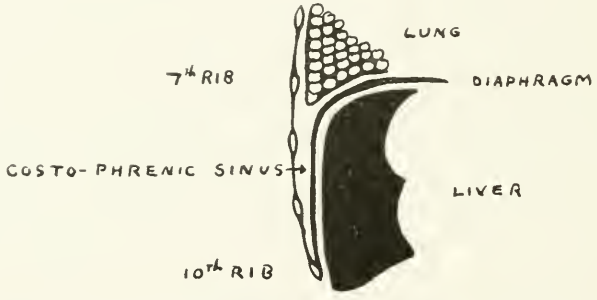

Fig. 2.—Diagrammatic sketch of the relation of liver and lung to the costophrenic sinus, in a frontal section made in the midaxillary line.

practical landmark of the lower limit of the pleural cavity, and the two layers of the pleura which line the costophrenic sinus lie almost in apposition.

When an empyema is present, this space is filled with pus, or, conceivably, may contain more fibrin than pus. While in the latter case the exploring needle might fail to reveal any fluid, the possibility of crossing the space and entering the diaphragm, and thus having a dry tap, is obvious. The serious consequences of traversing the diaphragm likewise are obvious, as on the right side the liver lies directly adjacent to the costophrenic sinus, separated from it only by the diaphragm, the parietal pleura and the peritoneum.

On the left side we found the upper border of the spleen, in the midthoracic line, lying opposite the ninth rib, or the interspace above or below it. In none of the bodies studied was the spleen greatly

enlarged. Puncture of the spleen from a careless tapping through the costophrenic sinus on the left side would be as liable to happen as would puncture of the liver on the right side. Increase in the size of the spleen naturally would increase the danger. A distended stomach also would lie directly underneath the costophrenic sinus, but unless the distention were extreme, would not lend itself easily to puncture.

We may say, therefore, that while the lowest level of the lung marks approximately the lowest level of the pleural cavity during quiet respiration, the optimum point for tapping the chest in infancy or early childhood should be somewhat higher than this level, in the interest of safe and conservative treatment.

According to Piersol[16] the lower border of the right lung in adults reaches the eighth rib in the axillary line, and the eleventh rib, or a little higher at the spine. The lowest portion of the lung is in the axillary line or a little posterior to it, but the line thence to the spine is nearly horizontal. On the left side the course is practically the same, although the left lung may descend a trifle lower at the side. Posteriorly, the lower borders are very symmetrical. Piersol further draws attention to the variations found in different types of chests, which will be referred to later.

In locating the lowest level of the edge of the lung in infants, we have selected two lines, (1) the midthoracic line and (2) a line dropped vertically from the apex of the angle of the scapula "at rest." This point is readily palpated in the living child. The results were as follows:

The lower edge of the lung in the midthoracic line on the right side was at the seventh rib or seventh interspace (7 cases), eighth rib (7 cases); on the left side it was at the seventh rib (4 cases), eighth rib or eighth interspace (9 cases), ninth rib (1 case). In the line of the angle of the scapula the lower edge was at the ninth rib or ninth interspace (12 cases), at the tenth rib (2 cases); on the left side the lower edge was at the ninth rib or ninth interspace (9 cases), tenth rib or lower (5 cases).

As would be expected, these results show that the lungs in infancy do not, on the average, reach quite so low as in adult life and corroborate Piersol's statement that the left lung reaches slightly lower than the right. We find, therefore, that the extreme lower edge of the

16. Piersol, George A.: Human Anatomy, J. B. Lippincott Co., Philadelphia, 1907, p. 1855.

lung, measured in the midthoracic line, in many infants does not extend below the seventh rib, while in the line of the angle of the scapula, in an even larger proportion of cases, the lowermost limit is the ninth rib.

The size of the liver, however, had less effect than would be supposed, since in the five cases which showed the greatest enlargement of this organ the lowest point of the lung in the midthoracic line reached the eighth rib. Although in the case with the smallest liver the lowest level was recorded as being at the eighth interspace, in two others with livers somewhat below the average size, the lowest levels were found to be the seventh rib and the seventh interspace, respectively.

An obvious objection which might be raised to the practical value of these figures fixing the lowest level of the lungs is found in the age of the specimens we examined, for the reason that empyema and pleurisy are comparatively rare in those under 1 year of age. We found, however, that in the oldest infant, one of 15 months, the level in the right side was at the seventh rib in the midthoracic line, while the lowest level, the eighth interspace, was found in an infant of only 3 months. Excluding these, the average age in five cases, in which the lower margin of the lung was at the seventh rib, was 3½ months, and in five others with the lower margin at the eighth rib, the average age was 3 months.

Since the costal, sternal and spinal diaphragmatic origins are fixed, and the development of the lungs and chest, as the child passes from infancy to adult life, is not only gradual, but also slow, it is probable that many children throughout the first decade will show the lowest level of the lung during quiet respiration at a point approximately as high as that found in some of these infants. The effect of deep inspiration at any age on the lower border of the lung of course is obvious.

In this connection we find that Piersol[17] states that the relation of the lower border of the lungs to the ribs is rendered very inconstant by the varying inclination of the ribs in chests of different sizes and shapes. We investigated this point in our studies, but we could not determine any definite relationship between the obliquity of the ribs and the lower border of the lungs. The examination of our specimens gave the following results:

When the angle of obliquity of the ribs in the midthoracic line

17. Piersol, George A.: Human Anatomy, J. B. Lippincott Co., Philadelphia, 1907, p. 1856.

was from 55 to 60 degrees, the lower border of the lung in the midthoracic line was at the seventh rib or seventh interspace in four cases, and at the eighth rib in two cases. When the angle was from 60 to 70 degrees the lower border of the lungs at the midthoracic lines was at the seventh interspace in one case, at the eighth rib or eighth interspace in three cases. When the angle of the ribs was from 70 to 80 degrees, the lower border of the lungs in the midthoracic line was at the seventh rib or seventh interspace in two cases and at the eighth rib or eighth interspace in two cases.

Although these figures indicate a tendency for the higher level of the lung to be found with the more vertical rib (55 to 60 degrees), the exceptions are too numerous to prove any definite relationship.

It would seem that the lowest point for tapping with absolute safety, therefore, would be the fifth or possibly the sixth interspace in the midthoracic line and the seventh or possibly the eighth interspace in the line of the angle of the scapula. In the authors' clinical experience it might be said that the sixth or seventh interspace in the postaxillary line (which lies between the line dropped from the angle of the scapula and the midthoracic line) is the optimum point of attack.

CONCLUSIONS

1. The fissures of the lung in infancy show practically the same relation to the bony framework of the chest as in adults.

2. The origin, course and termination of the fissures vary greatly in different individuals.

3. The variations apparently do not depend on any of the anatomic characteristics of the chest and cannot be predicted therefrom.

4. The lower level of the lungs in infants and probably in young children does not extend quite so low as in adults.

5. For this reason, and owing to the anatomic characteristics of the bases of the pleural cavities in early life, great care should be exercised to avoid damage to the diaphragm in performing thoracentesis.

6. The sixth interspace in the midthoracic line and the seventh or possibly the eighth interspace in the line of the angle of the scapula (at rest) represents the lowest limits of absolute safety for thoracentesis in early life.

THE COSTOCHONDRAL JUNCTION IN RICKETS*

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The normal rib is slightly enlarged at the costochondral junction on both the internal and external surfaces. The enlargement on the external surface can often be palpated and even seen, if the subject is sufficiently emaciated, and is often incorrectly regarded as being rachitic in nature for these reasons. The enlargement at the costochondral junction on the inner surface of the rib is always greater than that on the outer surface and sometimes becomes extremely marked in the middle tier of ribs, particularly if some form of chronic inspiratory obstruction is present.

Rickets shows itself earliest at those points in the skeleton where growth is occurring with the greatest rapidity, and consequently is found in the middle tier of ribs at a time when there is little or no evidence of it elsewhere. (Schmorl.)

Slight degrees of rickets produce no change in the configuration of the costochondral junction whatsoever, and even advanced forms of rickets may exist at the costochondral junction, particularly of the lower ribs, without producing any enlargement in excess of the normal.

Usually, however, well-marked rickets produces definite and characteristic gross deformities at the costochondral junction.

The rachitic deformities of the costochondral junction may be arbitrarily divided into four classes. In the first class of the least severe deformities there is enlargement on both the external and internal surfaces of the costochondral junction, but with the predominance on the internal surface. In the second group of deformities the junction of cartilage and rib is marked by a pronounced deformity internally, but with an absence of external deformity, that is, externally cartilage and shaft pass into each other without the production of any elevation which can be seen or felt. In the third group of deformities of the costochondral junction a large knuckle is found on the inner surface projecting into the cavity of the thorax, while the junction is marked externally by a depression into which the finger can be thrust.

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*Author's abstract of paper.

When these severe forms of rachitic deformity are analyzed, it is found that the bony shaft, at its tip, is beveled on the outer surface, and usually to a less extent on the internal surface also, so that it terminates in a sharp edge; and that the cartilage which, close to its junction, undergoes a club-shaped enlargement, unites, not with the end of the bony shaft, as of course is normally the case, but with the outer surface of the end of the shaft; and that the angle or gap which is thus left on the outer side at the point of junction of cartilage and bony shaft is filled in with a triangular mass of periosteum.

The costochondral junction in these severe cases has been transformed into a joint which flexes with inspiration and snaps back into a more extended position at the beginning of expiration. It is no wonder, therefore, that growth does not occur at the costochondral junction in the severest types of rachitic deformity.

Before growth can occur, it is necessary that the bony shaft acquire sufficient stiffness so that the costochondral junction is no longer displaced inward by the forces which are operative during expiration, and that the costochondral junction be reenforced by an abundant growth of periosteum in its external angle.

It is chiefly through the weakness of the rib at the costochondral junction in rickets that pigeon breast and the common combination of pigeon and funnel breast are brought about.

The fourth form of deformity of the costochondral junction is exactly the reverse of the several deformities already described. The costochondral junction points externally, so to speak, instead of pointing internally, and the cartilage joins the inner side of the end of the shaft instead of the outer side. Such external deformities of the costochondral junction are far less common than the internal deformities and occur probably only when severe rickets of the thorax is accompanied by inspiratory obstruction.

FINAL REPORT OF COMMITTEE ON VAGINITIS IN CHILDREN

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AND
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The report of this committee presented to the Society last year summarized the answers to questionnaires which had been sent to various persons and institutions throughout the United States. These formed the basis for two sets of recommendations, one to health officers, the other to hospitals which treat children. After more or less discussion these recommendations were approved by a majority vote.

A member of the committee then stated that he thought it would be detrimental to the best interests of the Society and its usefulness in this line of work for it to send out recommendations which had not the unanimous approval of its members. He therefore made a motion that final action be deferred for another year; that the committee be continued and that its members be privileged to gather whatever additional information might be desired to support the recommendations they had made, and further, that the action already taken be considered merely as an approval of the committee's work. This motion was carried.

This year the committee desires to present the recommendations again, with certain modifications, in the hope that they may receive the Society's official approval.

Last year the suggestion was made to one of the committee that the most important point to be determined concerning gonococcus vaginitis was whether or not the organism usually found in the vaginitis of children was identical with the gonococcus of the infection as it is found in the adult. The work of Louise Pearce,[1] which had been published shortly before the meeting at Lakewood, doubtless formed the basis for this suggestion.

In her immunologic studies of strains of gonococci she found dis-

1. Pearce, Louise: Jour. Exper. Med., 1915, xxi, 209.

tinct differences in agglutination and complement fixation reactions between the organism recovered from adults and that recovered from children suffering with vulvovaginitis.

She concludes, therefore, that two principal types of gonococci may be recognized by suitable immunologic studies, which correspond to the adult and infant types of infection with the gonococcus seen clinically. She qualifies this conclusion with the statement that the distinction between the two types is not clear cut and absolute.

Doctor A. Graeme Mitchell of Philadelphia has reviewed for us very carefully the literature for the last five years, but could find no reference to any other work of like nature in which the modern immunologic reactions have been studied in the attempt to differentiate various types of gonococci.

The committee greatly desired to have a further and more comprehensive study made, but were unable to do so, partly from lack of funds necessary to carry out the work on an adequate scale and partly because no competent volunteer worker could be found who was willing to devote the necessary time to it.

Failing to find a worker, the committee appealed to Dr. Flexner and was glad to learn that he was already interested in the problem to the extent of including it among the studies to be undertaken at the Rockefeller Institute. We are permitted to announce that work is now in progress which, it is hoped, may help better to define the bacteriologic nature of the disease.

So far as the technic of cultural methods is concerned, the evidence seems to be in favor of the belief that the gonococcus can be isolated and recognized from whatever source obtained.

In a recent report on the diagnosis, prevention and treatment of vulvovaginitis in contagious disease hospitals, from the Research Laboratory, New York, Anne W. Williams and M. A. Wilson seem to have no doubt as to the presence of the true gonococcus in many of these cases.

Dr. William B. Wherry, of Cincinnati, in a private communication, stating the results of studies which he has been making during the past winter, has found no cultural differences between the organism recovered from an adult male with gonorrheal urethritis and those from cases of vulvovaginitis in girls. Even so long ago as 1895 our confrère Dr. Heiman[2] described the successful growth on chest serum agar of a

2. Heiman: Med. Rec., New York, June 22, 1895.

gonococcus recovered from a case of vulvovaginitis in a girl, "which differed in no respect from the organism found in the adult."

Dr. Carl C. Warden from the Hygienic Laboratory, Ann Arbor, writes:

"Whatever may have been my ideas formerly, my studies in the last two years of the cases in the Palmer ward here in Ann Arbor, and those in the annex of Cook County Hospital and at the Home for Crippled Children in Chicago have shown me that in most of them the gonococcus of Neisser was responsible primarily. In all the cases the diagnosis was made both from cultures and complement fixation. I was never able to determine any variation in characters of these strains from those isolated by me at the same time, and at other times, from cases of specific urethritis in adult females and males. A small proportion of cases of vaginitis in cachectic, crippled and bedridden children were repeatedly negative to cultural and complement fixation tests."

We may again note the opinion of American bacteriologists expressed in last year's questionnaire. Twenty-six out of thirty-four believed that the gram-negative intracellular diplococcus found in the vulvovaginitis of childhood is the true gonococcus in 75 per cent. or more of cases.

Furthermore, it is unquestionable that vulvovaginitis in childhood frequently owes its inception to direct or indirect contact with a true gonococcal discharge as it exists in adults, and that this infection, in any individual child, often involves subsequently a whole series of babies and girls in hospitals, homes, day nurseries, etc. The clinical symptoms are the same both in the originally infected child and in the subsequent contacts.

It may be found that the passage of this adult type of organism through a series of children profoundly affects its characteristics and virulence. On the other hand, numerous clinical experiences seem to prove that the organism found in cases of vulvovaginitis after repeated contact infections from girl to girl possesses undoubted virulence. For example, in the personal experience of one of the committee, a girl of 5 years, six weeks after admission to a hospital, when convalescing from a mild attack of pertussis, developed a vaginal discharge. Examination of smears demonstrated gonococci. A day after the vaginitis was discovered a conjunctivitis developed in one eye, and the bacteriologist reported gonococci present in the discharge. In spite of continuous treatment, in forty-eight hours the cornea perforated with resulting complete loss of vision in the infected eye. At the time this child developed the vaginal discharge there were two other children

in the isolation department with vaginitis and all the evidence pointed to infection from this source.

As a rule, however, it is undoubtedly true that children seem to possess greater immunity to serious systemic infection than adults. Whether this depends, again, on the lowered resistance of the micro-organism, on certain immunologic substances in the child's blood, on anatomic peculiarities, or on a combination of these factors, remains to be determined.

Notwithstanding the fact that, in relation to the number affected, the proportion of serious complications, sequelae, fatalities and the contact infection of nurses is small, yet we must not lose sight of the fact that the disease vaginitis is not to be regarded lightly. One of the serious indictments against it is the demoralization of the service caused by a hospital epidemic, and the fact that the presence of vaginitis so frequently interferes with the admission to children's hospitals of patients who are urgently in need of treatment.

In the registration area during 1914, which included 66.8 per cent. of the total estimated population of the United States, sixty-four deaths of children under 10 years of age were reported as due to gonococcus infection. Since vaginitis and ophthalmia neonatorum are the chief types of gonococcus infection in children, and the latter is rarely fatal, most of these sixty-four fatalities probably followed infection through the vaginal route, and are much more impressive than the figures elicited by last year's questionnaire.

Whatever the result of further bacteriologic and serologic studies may be, the committee feels, therefore, that such a contagious, repulsive, degrading, and at times, dangerous disease demands more active measures to prevent its spread, and that action on the various recommendations is most desirable.

The committee has sent a copy of the resolutions which were presented and adopted last year to every member of the Society, requesting comment.

Replies were received from 64 members: Eighteen approved of the recommendations in toto; fifteen approved of the recommendations to hospitals, but made some suggestions or objections to one or more of the recommendations to health officers; six approved of the recommendations to health officers, but suggested some modification for the recommendations to hospitals; the remaining twenty-five modified in some particulars both sets of recommendations.

The Committee, in repeated discussions of the original recommendations, had decided on several modifications, irrespective of these suggestions. These will be indicated, seriatim, and followed by the suggestions made by other members. The committee also has some new recommendations to propose. Finally, under many of the headings we desire to present arguments in their favor with certain explanatory data.

You will recall that last year the committee made the recommendation that the American Pediatric Society address a special letter to health officers relating to the control of vaginitis. This recommendation was duly adopted.

In response to the letters sent to the members of the Society this year asking for comment on the original recommendations, several have expressed opinions in regard to the desirability of addressing health officers.

One, approving of the purpose, sounds a note of warning that, with the exception of the larger cities, it will take a number of years and a great deal of agitation to enlist the active aid of health officers and boards of health.

Another, believing that vulvovaginitis in little children is more of a nuisance than a danger, thinks that too much stirring up of this question among physicians in general may produce an entirely unnecessary tenseness of feeling with regard to it. Moreover, he believes that addressing a letter to health officers should be considered most cautiously since physicians often suffer decidedly from the overactivity of their officials.

A third suggests that the letter be sent to state boards of health as well as to city officials so that the latter may receive proper support in states in which the Commonwealth has jurisdiction over the municipality in matters of health.

The first recommendation made in the proposed letter to health officers in last year's report was:

"A. That cities be compelled to make adequate provision for the care of cases of vaginitis."

This recommendation was adopted.

The committee desires this year to present a modification as follows:

That cities be required to provide adequate hospital and dispensary facilities for the care and treatment of children having vaginitis.

In criticism of the original recommendation several members objected to the word "compel." The committee has substituted the word "require," as sounding less harsh, but it should be noted that the "compulsion" would be enforced by the health officers, not by the Society.

One member calls attention to the danger of compelling hospitals to admit patients with vaginitis, unless the type of nursing be adequate for their efficient care and management. This is a sound objection, if patients are to be admitted to the general wards, but loses its force in part if the recommendations to hospitals be taken into consideration; and if the term "adequate" be literally interpreted.

Another believes that patients are best handled at home under proper supervision. Granting the latter factor, this is probably true, but this method does not provide for those children who need hospital treatment and at the same time are suffering from vaginitis. The necessity of providing for such children is obvious. Both of these members evidently prefer dispensary treatment to hospital treatment for cases of vaginitis per se.

Fifty-six members approved of the original recommendation, and another member approves for "dispensary patients whose parents are willing." Apart from those noted above only three members disapproved of the recommendation.

So far as we can learn there are only six hospitals in the country which at all times maintain a special ward for patients with vaginitis; three in the East and three in the Middle West. In seven cities patients are admitted to the city hospitals and isolated, but no special provision is made for them. Two other cities admit them to their isolation hospital and another apparently utilizes its venereal wards for cases of gonococcus vaginitis in children.

Apart from Philadelphia, we find that in six of the largest cities in the United States there are only thirty beds which are especially maintained and designated for cases of vaginitis. The situation in Philadelphia warrants a description.

The Philadelphia General (City) Hospital has maintained since 1903 special beds for patients suffering with vaginitis. Gradually they have been increased until they now number fifty-two, and have been grouped into one department, comprising one entire floor of the Children's Hospital building. It is known as the Children's Infectious Ward. This floor is used exclusively for the care of these children.

There is one large ward with sun parlor, seven small wards, each with a capacity of three or four beds, a play room, one bathroom equipped for spray bathing, and another bathroom with shower baths for the older children. There are two treatment rooms, one operating room with autoclave, a sterilizing room with steam utensil sterilizer and water sterilizer, a linen room and a diet kitchen. In addition a special section of the yard is set apart for these children, which is isolated from that used by the other children by a double fence, and is entered from a separate fire-escape. The patients in the Children's Infectious Ward have a different intern from the other children in the hospital, and are cared for by day and night nurses who do not come in contact with the other patients in the building. No visitors are admitted. The patients have individual toilet articles, thermometers and catheters, and single service diapers. Children with negative smears are separated from those having positive smears pending the final decision as to their recovery.

Children with vaginitis are admitted to this infectious ward whether they are suffering from vaginitis only or vaginitis and other diseases.

All of the forty-eight patients with vaginitis in the infectious ward at the time this report was written were suffering with the disease at the time of admission. The majority of them contracted the disease in other hospitals and were sent, because of the vaginitis, to the Philadelphia Hospital, as this is the only hospital in the city which continuously provides accommodations for such cases.

Judging from our experience in Philadelphia, where we have seen the problem presented by vaginitis slowly but surely increasing from year to year, we feel that other municipalities may be confronted by a like problem unless adequate precautions are taken.

In the experience of all the members of the committee, a large number of cases of vaginitis owe their origin to infection in the general children's wards of hospitals, and we feel that too much care cannot be taken to impress on the authorities the danger of allowing patients with vaginitis to be cared for in general wards. The safest plan is the maintenance of separate wards and separate dispensaries.

"B. That children with vaginitis be excluded from school."

This provoked considerable discussion and was finally passed, sixteen for and eleven against.

The Committee desires to present the following modification:

That children known to have gonococcus vaginitis be excluded from

schools and not readmitted until the receipt of a physician's certificate stating that he has examined the child once a week during a period of three weeks and that there has been no discharge during this time.

Forty-one members approved of the original recommendation, two specifying that gonococcus vaginitis be intended. Two others believed that exclusion would be necessary only for selected cases, two believed that exclusion should be enforced only during the stage of active discharge, and two approved, but feared that public opinion would not sanction it.

Thus forty-seven members seem to be in favor of exclusion, while seventeen object more or less to it.

The objections to the recommendation may be grouped as follows:

1. Exclusion not warranted by the severity of the disease.

2. That the course of the disease is so chronic as to materially affect the education of the child were exclusion insisted on, unless special schools or classes were maintained. The latter extremity does not seem to be warranted by the severity of the disease.

3. Objection by parents. This would mean that they would attempt to hide the fact that their children had vaginitis and would not avail themselves of the opportunity of having it treated at dispensaries and hospitals.

4. The fact that open toilet seats and supervision in the toilet rooms, if adopted, would obviate the necessity for exclusion.

Objection was also made to having children examined by the school physicians. The modification of the recommendation obviates this criticism.

In this connection the report contained in the weekly Bulletin of the New York Department of Health was cited. In two Brooklyn schools smears were made from the inner edge and front surface of an ordinary toilet seat. Cultures in ascitic broth and blood broth and coverslip preparations from the smears failed to reveal gonococci.

Unfortunately the report does not state whether or not the toilet had been used by children suffering from gonococcal vaginitis. Obviously, also, the length of time elapsing between contamination and making the culture must influence the result.

It would not require a laboratory test to prove that infection would not only be possible but highly probable, if an uninfected child were to use a toilet seat a few minutes after it had been smeared with

gonococcal pus, unless she took extreme precautions to avoid touching the front of the seat.

Until it is demonstrated that the gonococcus discharge loses its infectivity within a few seconds after it is smeared on a plain, hard surface your committee is bound to consider toilet seats a possible source of contagion from which children should be protected. That the U-shaped toilet seat would obviate many of the dangers seems highly probable, but other dangers exist, for example, the ease with which one of the ordinary desk seats or benches could be contaminated by the profuse discharge seen in the active stage of the disease. It is also true that a small child could not safely use a high seat, even if the front end were open, and it must not be forgotten that the recommendation to install proper seats will be observed by comparatively few schools for a number of years.

With regard to maintaining separate schools or separate classes for infected children, the difficulties are clear. The stigma which would be attached to the children unquestionably would be most unjust, and it is hard to believe that education of the laity will ever be able to justify it. That no attempt has been made in sixty-two states and cities to maintain separate schools was also learned from our questionnaire of last year.

In the attempt to throw further light on the problem as it affects school children the following questions were sent to:

First, chief medical school inspectors in cities with a population of 150,000 or over.

Second, superintendents of schools in cities with a population of 100,000 or over.

Third, supervising school nurses in cities with a population of 300,000 or over.

The questions to the chief medical school inspectors were as follows:

1. Are children known to have vaginitis permitted to attend school? If not, how are the cases recognized?

All those who answered this question, twenty-six in number, stated that children known to have vaginitis are not permitted to attend school. The sources of information about the cases, in the estimated order of importance are: family physicians, 42 per cent.; hospitals and dispensaries, 30 per cent.; nurses, 11 per cent.; teachers, 8 per cent.;

and the children themselves, 8 per cent. (This estimate is based on the number of times each factor was mentioned in the replies.)

2. What means are taken to prevent the spread of vaginitis in schools?

In most instances chief reliance seems to be placed on exclusion from school and especial care of the toilets.

3. Is examination of children by a trained nurse for the presence of vaginitis to be recommended?

Most of the answers are opposed to routine examination by a nurse, on account of unfavorable public opinion or because it would discredit the good work that is being done and bring the system of medical school inspection into disrepute. A few are in favor of it and more advocate it for suspected cases only.

4. Is an exclusion law to be recommended?

Eleven are in favor of such a law, ten state that existing laws confer the necessary authority to exclude, one would favor it if vaginitis were prevalent, and only one is opposed.

The question to the superintendents of schools were as follows:

1. To what extent is vaginitis a problem in your schools?

2. How is it discovered and how is its transmission prevented?

3. Would it be feasible to place matrons in charge of the toilet rooms?

From the answers received to these questions it is evident that, so far as the superintendents are aware, vaginitis is not a serious problem in schools, as few cases are called to their attention. The school nurses seem to be the chief agents in discovering cases. The answers to the last question will be noted later.

The questions to the supervising nurses were as follows:

1. Do school nurses examine for the presence of vaginitis in suspected cases? If not, would it be desirable?

2. How many cases have been called to your attention?

3. Where were the cases contracted?

The school nurses, as a rule, do not make examinations nor do they believe it to be desirable that they should. In one city in the Middle West an epidemic of 100 cases occurred in the schools last year; otherwise the number of known cases is small, averaging one to two a year in each school. Most cases are believed to be infected in the homes of the children, a few in hospitals.

The answers of the chief medical inspectors in some of the larger cities are worthy of reproduction, as they show the attitude of the authorities toward the problem and some of the difficulties inherent to it.

From a health officer in a city in the east:

"We do not take direct measures to detect the presence of the disease, as school medical inspection can be performed only in such manner as does not remove the child's clothing, unless the specific consent of the parent is obtained. Our efforts to check the transmission of the disease are therefore confined to measures taken after a case has been reported to us. These measures include the formal exclusion of the child until its guardian produces a medical certificate of recovery, including the statement that smears have proved negative; also the toilets of the school are scrubbed with disinfecting solution."

From a Health Officer in a city situated in New York State:

"Not only are children with vaginitis excluded from school, but most of them are not permitted to remain at home. Under the law, whenever cases are discovered, the attempt is made to induce the parents to send the child to the hospital. If the family is ignorant, careless, stupid, or wilfully negligent, the child is then committed under Section 326 A, of the Public Health Law of New York State, which provides that a person suffering from an infectious disease or a carrier of such a disease, unwilling or unable to conduct himself so as not to expose members of the family or household or other persons, may be committed to a hospital by a magistrate.

"If the following plan meets with the approval of the superintendents of schools, as it doubtless will, every schoolchild reported by the teacher as in any way suspicious, either by marked odor about the clothing, frequent desire to go to the toilet, or because of suspicious actions, will be interrogated by the nurse. The nurse will then inquire of the mother whether there is reason to believe that the child has any irritation about the genitals. The nurse will then try to get permission from the parents to make a vaginal smear, and the report of the case will be returned to the health bureau. If gonococci are found in the smear provision for adequate treatment will be made, if the parent fails to provide such treatment through the family physician."

From a health officer in a city in New England:

"The cases were discovered at clinics, as the school physician is not supposed to make local examination of children. Local examinations of children by school physicians are highly inadvisable for various reasons. The rule is that no child in whose vaginal discharges gonococci could be demonstrated should be allowed to attend school, and that no child should be regarded as cured until there have been three negative examinations at a month's interval. This hard and fast rule meant the excluding of a great many children who were practically cured, although the gynecologists would not commit themselves to saying they were. At present the matter is usually left to the discretion of the chief of the clinic at which the child is being treated. All children having this infection should be kept from school for a few weeks. Clean, intelligent children should be allowed to return to school, especially when they live near enough to the school to be allowed to return home to use the toilet.

It is not advisable for careless, dirty or vicious children to return to school until completely cured. In cases of this kind the teacher or head master should be notified as to the condition of affairs. It is advisable and desirable that children should report occasionally to their respective clinics until several negative smears have been obtained. There is not yet a single case reported of gonorrhea developing as a result of allowing selected cases to return to school while the infection is still active. It would be deplorable to allow indiscriminate attendance at school of girls with gonorrhea."

From a health officer in another city in New England (after giving history of cases):

"These cases you will note were not discovered by the school physician, but by outside agencies. They were reported to me through the various social workers with whom we are in close cooperation. The source of infection I feel was not in the school in any of the cases, and I do not feel that there is great danger of transmission through the school, but our policy is to exclude any schoolchild who we know has gonorrheal vaginitis until she is shown to have two negative smears."

From a health officer in a city in the South:

"We have not taken any definite measures to prevent its transmission from an infected child to its schoolmates. Our school inspection system is quite effective, much more so probably than the average city of our size. We have nine school nurses, six white and three colored. The school nurses devote their entire time to the work. We also have sixteen school inspectors who devote part of their time to school inspection. Both our doctors and nurses have special instructions with reference to the inspection constantly of toilet facilities and we have good reasons to believe that these facilities are up to the average, both in point of equipment and maintenance. Your letter has done at least the good of directing our attention to this matter and it is possible that we may make some tests along the lines indicated. We will be pleased to know of your work in this direction and especially any activities in which you may engage."

From a health officer in a city in the West:

"Our system of inspection consists in heart to heart talks with the mothers at their homes and at parent-teachers' meetings held monthly. All of our school and home inspections are made by trained nurses, especially trained for this purpose. We have no medical men in connection with the examination of the children in the schools. We have a public school clinic, however, to which all the children of the poor are sent for diagnosis and treatment. The children of the well to do are sent to the family physician. The nurse in connection with her work discusses this question of vaginitis with the mothers and makes the examinations. Their findings are reported to me, when treatment is instituted usually at the home, sometimes at the clinic, depending on the severity of the case."

Further comment would seem to be unnecessary. Vaginitis may have been, on the whole, an insignificant problem in the school, but the experience of a middle western city last year, in which a school

epidemic of 100 cases was encountered, at least points to the possibilities and it is difficult to see how we could do less than recommend exclusion of active cases when the chief medical school inspectors themselves are almost unanimously in favor of it, unless the Society comes to the conclusion that the interference with the sick child's education by reason of exclusion outweighs the importance of safeguarding the uninfected child.

"*C. That matrons be placed in charge of the girls' toilet rooms in public schools.*"

This recommendation was discussed and adopted, and the committee has no change to suggest.

Fifty-five members approve of it. The two chief objections are that it would be unnecessary or that the expense would be too great. While the latter factor would be prohibitive in many cases, it does not seem to be a valid objection to the recommendation provided that the matron would perform a useful and desirable function.

The committee believes that a competent matron would not only keep the toilet room in a sanitary condition, especially the toilet seats, but would also act as a "censor of morals," a rôle which probably would be eminently desirable. It is not hard to imagine that the right type of woman would have a most wholesome moral effect in an atmosphere which, from the ethical standpoint, is often far from pure.

The answers from the superintendents of schools as to the advisability of having a matron placed in charge of the toilet rooms may be summarized as follows:

One city in the West has a matron in charge of the toilet rooms in each of the high schools and the superintendent approves of the plan Another believes it to be a wise move, basing this opinion on a general knowledge of the disease (vaginitis) and its prevalence in unsuspected quarters. In two cities teachers have charge of the toilet rooms during recess, and in another city a teacher is regularly appointed to oversee the toilets, teachers serving alternately in this capacity. The toilets, therefore, are under constant supervision.

Another superintendent thinks well of the plan in general, but believes it to be unnecessary so far as vaginitis is concerned. Two others believe it to be entirely unnecessary. In four cities the superintendents approve in theory but think that the practical good accomplished would not warrant the expense. Four others simply object on the grounds of expense.

From this investigation we may conclude that school superintendents as a rule do not consider the matron a necessity. This is probably in line with their opinion with regard to vaginitis.

The committee feels that the expense of maintaining a matron in charge of school toilet rooms would be warranted on the following grounds:

First, improvement of the general sanitary condition of the toilet rooms.

Second, prevention of the spread of infectious diseases, including vaginitis.

Third, protection of morals.

"D. That U-shaped toilet seats be used in all schools."

This recommendation was adopted almost without discussion.

The committee desires to suggest the following modifications:

That toilet seats embodying the principle of the U-shape be used in all schools and that the toilets be of proper heighth for different ages.

Only one member opposed the use of the U-shaped seat, but failed to express any reason for his disapproval.

Even the U-shaped seat would not entirely obviate the dangers of contamination by vaginal discharge unless the height of the seat be adapted to the size of the child. This open-end seat of suitable height would seem to afford the greatest possible protection. The only argument involves the selection of the type of seat. That style which is open both front and back possesses certain advantages over the simple U-shape.

"E. That city and state laboratories be equipped to make bacteriological examinations for private physicians."

This recommendation was discussed and adopted.

The committee desires to modify this recommendation as follows:

That city and state laboratories be empowered and equipped to make bacteriological examinations for physicians when patients cannot afford to pay a private laboratory fee.

Except for the provision that such examinations should be made only for patients who are unable to afford a fee for the services, there seemed to be no objection to this recommendation.

As a matter of fact such equipment is already provided in many cities and states, fifty-eight of sixty-seven heard from last year stating that they were prepared to make bacteriologic diagnoses from microscopic

preparations sent by private physicians. Twenty-six out of sixty-one laboratories also were prepared to make complement fixation tests.

"F. That educational literature on the subject of vaginitis be prepared and distributed."

This recommendation elicited considerable discussion before its final adoption.

The committee desires to present the following modification of this recommendation.

That educational literature on the subject of vaginitis be prepared and distributed to mothers through the medium of physicians, hospitals dispensaries, health centers and municipal visiting nurses.

Forty-two members approved of the original recommendation without comment. Of the remainder a number specified that the literature should be very carefully prepared, and others, that it should be distributed only to physicians, nurses and school principals, and not to the public. A few approved of educating the laity, as one member expressed it, "in order no longer to be guilty of the charge that parents are not told of the danger and prevalence of the condition." Eight disapproved altogether of the recommendation, or could see no necessity for it, one basing his objections on "the belief that the literature probably would not accomplish much; would give prominence and notoriety to what is best handled individually and would, perhaps, rouse an undue fear in the minds of many people."

According to last year's questionnaire only three states and none of the cities were distributing any literature on the subject of vaginitis in childhood. One state had prepared a pamphlet, but owing to "outside influences" was compelled to withdraw it.

Further inquiry this year shows a distinct increase in the amount of interest taken in the subject of education. Six states and three cities are preparing or have issued literature, or are giving instruction to mothers in lectures, and four others have made a request for sample literature.

It seems to the committee that the possible harm which the distribution of carefully prepared literature might cause would be far outweighed by the amount of good which could be accomplished in the crusade for enlightenment, without which progress in prevention will be seriously hindered.

"G. That gonococcus infection be made a reportable disease."

This recommendation was adopted and the committee desires to recommend it again without modification.

In answer to our request this year, members of the Society have criticized it much more freely than was done at the meeting.

Thirty-six approved and five disapproved, without comment. One approved because "without knowledge of its extent we cannot control the disease." Another approved for children living under poor hygienic conditions who are attending public schools. Another sanctioned the recommendation, but doubts whether the public will permit the law to be enforced. One is "uncertain of the hardships which may result, but feels that less may not suffice."

Another approves, if names are suppressed, otherwise fears it would tend to make parents conceal the existence of the disease. For the latter reason another disapproves and is "inclined to think that the control of the disease should be in the hands of the physicians of the community rather than in those of a public board of health."

Six members think the desirability of such a law is debatable, chiefly because the public is not ready for it. Two believe that failure to comply with the law will nullify its advantages and they believe that it would place an unjustifiable stigma on the child. One is opposed because the law would give too much encouragement to blackmail and attention from quacks, and another believes that we should await the results of further bacteriologic studies of the gonococcus. Another thinks that the law in general could not be enforced, but approves of having institutions, hospitals, homes, asylums and day nurseries report their cases. Another disapproves, believing that physicians should not be placed in the position of violating the law or of becoming subject to the danger of action for damages. With regard to having institutions report vaginitis, such action could only be voluntary on their part, in the absence of a general law. Special laws covering institutions only would be unconstitutional.

According to the United States Public Health Service gonococcus infection is a reportable disease in ten states, and ophthalmia neonatorum in twenty-four others.

A letter was sent the chief of the bureau of vital statistics in each of the forty-eight states, asking for the number of cases of gonococcus infection in childhood reported during 1914.

The chief health officer in a city situated in the state of New York states that gonococcus infection in children is reportable and that

twelve cases were returned during 1915. He admits that this does not represent the total number of cases which occurred, but claims that physicians are glad to cooperate whenever they discover cases, and that the ordinance is satisfactory.

In one middle western state which makes venereal diseases reportable 281 cases of syphilis and 843 cases of gonorrhea were returned in 1913-1914. Of the latter, six were cases of gonorrhea in children under 9 years of age and ninety-six in children from 10 to 19 years of age. In 1914-1915 only two cases in children under 12 years of age were reported.

In another middle western state venereal disease was made reportable only in 1914, and cases are reported by number. This makes it difficult to enforce reports and the authorities have not been very insistent. The campaign for reporting has been one of education rather than legal compulsion. Last year only fifty-eight cases of gonorrhea were reported and of these only one was in a child, an 11-year-old girl.

In a western state which requires that all cases of venereal disease be reported it has been found impossible to secure enforcement of the law, which is practically a dead letter.

A second western state has only recently required the reporting of gonococcus infection and therefore no figures are available.

From an eastern state there were reported 301 cases of gonorrhea in 1913, 1914 and 1915, and of these nine were in children under 12 years of age.

To sum up then, we have definite information that gonococcus infection is a reportable disease in ten states and in one city outside of these states. In one state the law is frankly disregarded, in another state in which reporting is done by number the law is indifferently observed, in two others reports are made evidently only by a small minority of physicians, judging by the disproportion between returns and a low estimate of the actual number of cases, and in the fifth state the law is of too recent enactment to allow of judgment as to its efficiency.

In one city the law is satisfactory so far as the children are concerned, although the number of returns, again, must be below the actual number of cases.

From the figures of only one state can we judge of the proportion of adult to children's cases, 292 to 9, or 32 to 1. This proportion probably is much smaller, since many physicians would not look on

the vaginitis of childhood as reportable under a venereal disease law. In view also of the probable large number of unreported cases among adults, the number of cases in children must be painfully large.

In a letter from the health officer in a southern city we learn that the board of health is contemplating the enforcement of a physical examination of all domestic servants. Particular interest is attached to determining that they do not have gonorrhea or syphilis. From the histories of several cases "the evidence seems pretty conclusive that many of the children have been infected by negro maids."

On the whole the evidence shows that the enforcement of a law to report gonococcus infection would be extremely difficult. On the other hand, it must be remembered that the campaign for enlightenment of women, who, with the children, are the chief sufferers from the effects of gonococcus infection, is still in its infancy. The committee believes that such a law eventually will be enacted in all the states. The recommendation would serve to place the Society in the van instead of allowing it to remain in the rear of the procession which the passing of time will witness.

This completes the list of recommendations to health officers which were proposed at the last meeting. The committee desires to present an additional recommendation, as follows:

H. That asylums for children and day nurseries be licensed, and that the license be not granted unless, first, the institution has adequate facilities for the recognition of gonococcus vaginitis, and second, that the institution excludes children having this disease if they cannot be properly isolated.

In the general discussion a year ago on the proposed letter to health officers at least two members of the Society expressed the belief that institutions such as asylums and day nurseries were important distributing centers for gonococcus vulvovaginitis and that they should be licensed, but that the permit to operate should only be granted when they possess means for the recognition of the disease and for the proper segregation of patients.

Your committee in attempting to secure more data on the prevalence of the disease in day nurseries has been surprised to find comparatively little evidence of it in these institutions. In twenty-seven nurseries in New York City and Philadelphia, with a daily attendance of about 1,536 children, only fourteen cases of vulvovaginitis have been observed in the past year.

Very probably a number of instances of vaginitis have been overlooked, as only a very few of the nurseries require a negative smear before admitting a child. In sixteen of the establishments a physician makes the preliminary examination, and in seven he also examines all children at stated intervals; in ten others a nurse or matron, who has been especially instructed, makes repeated (often daily) inspections for the presence of a discharge.

Within the last two weeks the physicians of the Philadelphia day nurseries have, at the request of your committee, made special examinations of the girls and have found no evidence of the disease, except in one institution, in which a case had been previously detected. Smears were made from the other children by the board of health and two positive cases were found.

Although individual instances of the disease have undoubtedly been unrecognized, it seems unlikely that this number is large, else there would be numerous epidemics which could scarcely be missed, even by a matron of mediocre intelligence. We have records of only four such epidemics.

Of four hundred and eight cases of vaginitis that have been investigated as to their etiology by trained social workers or by visiting nurses connected with hospitals, only five cases have been traced to day nurseries. All of these were reported from one city, and in fact by one hospital.

The chief of the division of institutions and child caring agencies of the department of health of New York City writes that "3.8 per cent. of all female children admitted to the day nurseries of New York City during 1915 had visible signs of vaginitis. Smears were made from all these patients. Only 1.8 per cent. of these were reported positive (representing one case in every 1,470 children), 6.3 per cent. were doubtful, 0.9 per cent. suspicious and 91 per cent. negative."

The strongest evidence of the prevalence of this disease in day nurseries that your committee has obtained is a summary of the records of a large clinic in New York City. Eight hundred and seventy-seven cases of vulvovaginitis were investigated as to the sources of the infection, and in 14.50 per cent. this was traced to day nurseries. In explanation the chief of the clinic writes:

"This percentage seems high, it is true, but I recall one day nursery which sent us eleven cases within a month. Another factor may be the neighborhood; there are four day nurseries in the clinic district. The visiting physician to one of these nurseries makes a routine examination for vaginitis once

each month of all inmates. This is in addition to entrance examination. Supervising nurses of day nurseries are on the lookout for any suspicious vaginal discharge more than formerly."

With the exception of this report the evidence we have been able to obtain indicates that day nurseries, as they are at present conducted in New York City and Philadelphia, are not factors of great importance in the spread of vaginitis. Nevertheless, your committee believes that the disease would be found more frequently if the inmates of all the nurseries were examined at short intervals by physicians or by specially instructed nurses, and if smears were more commonly made. But even if the facts here presented represent the true state of affairs, they amply justify the enactment of laws that will give health officers authority to establish regulations for the protection of the inmates of children asylums, infant homes, day nurseries, etc., against the ravages of this loathsome disease.

The health officers of fourteen cities of over 300,000 population were asked if the day nurseries in their cities operate at present under a license. In four cities either a license or a permit with definite regulations is issued. Four are at present drafting an ordinance. Two hope soon to have rules and regulations governing such institutions. None of the health officers of the remaining four cities could see any objection to requiring these institutions to operate under a license.

Last year the committee also recommended that the American Pediatric Society address a special letter to hospitals which care for children, containing certain recommendations. We now present the original list with modifications the Committee desires to suggest:

"A. That all hospitals which care for children be urged to admit cases of vaginitis for proper treatment with due protection for the other patients, preferably in separate wards."

This recommendation was adopted.

The committee desires to present the following modification:

That separate wards be maintained for the treatment of children with vaginitis who are also suffering from other diseases.

Forty-five members approved of the original recommendation, two disapproved, two were in doubt as to its wisdom, two considered it impracticable, two considered it unnecessary when proper technic and disposition of cases in the general wards are observed, and one considered that the care of such patients lies within the province of municipal hospitals.

Six others consider that separate wards are essential, and should not be optional, and two consider that the disease should be treated only in separate buildings or properly constructed separate wards. One approved of separate wards if cases cannot be treated at home or in a dispensary. One approved of separate wards in all communities in which vaginitis is prevalent, and another approved with the warning that the ladies' committees of hospitals will probably antagonize the recommendation.

The committee is more strongly in favor of separate wards than ever, as will be indicated by the change in the recommendation. The gross injustice of infecting, with a new and offensive disease, children who have been sent to a hospital for treatment of various other maladies is abhorent. The belief that vaginitis can be successfully isolated in the average general children's ward as it obtains throughout the country is a dream of the hardened optimist.

"B. That microscopic examination of smears be made before admission."

After some discussion this was adopted.

The committee desires to modify it as follows:

That microscopic examination of smears be made before admission to the general wards of the hospital. In securing material for the smears extreme care should be taken to observe rigid aseptic precautions.

Sixty members approved of the original recommendation. Three members do not believe that smears should be made routinely unless discharge is present or the history excites suspicion. One approved, but suggests that the best method for obtaining smears should be designated.

The committee believes that the best method for routine use is the irrigation-sedimentation method, introducing a small quantity of weak bichlorid of mercury in normal salt solution (1 to 5,000) by means of a small glass syringe or pipet and immediately examining the centrifugalized sediment. It fears to suggest this to all hospitals, however, as the technic should be perfect lest harm be done. On the other hand, to place reliance on the presence of demonstrable discharge or the reliability of the history we believe would be unsafe.

"*C. That observation wards be provided.*"

This recommendation was adopted and the committee has no change to suggest in this recommendation.

Fifty-eight members approved of it. Two approved, but believe it might be considered superfluous, since "every well-regulated children's hospital or department must have observation wards." To offset this, two others believe them to be unnecessary. A fifth thinks that the recommendation would not be followed and therefore could be omitted. Another believes in the system not so much on account of vaginitis as to exclude other conditions. A seventh prefers the small ward unit to the observation ward, as the stay in the hospital of most patients is short.

So far as vaginitis is concerned, the committee believes that an observation ward in which all cases are looked on as potentially contagious is the safest place to admit a girl until she has been found to be free from latent gonococcal infection. In our experience a distinct proportion of cases of vaginitis develop symptoms within the first few days after admission.

"D. That individual utensils, such as syringes and toilet articles, such as soap, powder and lubricant, be provided."

This recommendation was adopted.

The committee desires to suggest the following modification:

That individual syringes, bedpans, catheters, clinical thermometers, thermometer lubricant, wash basins, soap, powder, wash cloths, and towels be provided.

Sixty members approved the original recommendation without comment. One believes that the theory is good, but the practical accomplishment may be difficult. Another thinks the recommendation is so general and inclusive as to lose force. A third considers that individual utensils at the present day are supposed to be at the disposal of every child in every hospital for children. A fourth, in approving, expresses the opinion of the committee: "Because experience has clearly shown that without such detailed precautions the disease cannot be controlled."

"E. That single service diapers be used, at least for girls."

This recommendation was adopted after some discussion.

The Committee desires to suggest the following modification:

That single service diapers be used, at least for girls; or that diapers be sterilized in an autoclave at 15 pounds pressure for five minutes.

Fifty-four members approved of the original recommendation, one specifying that single service diapers are absolutely necessary. One approves only for positive or suspicious cases; another believes them

to be unnecessary, and a third objects on account of the expense. Six others believe that thorough disinfection of, or boiling, the ordinary diapers is sufficient precaution.

In an effort to determine to what extent single service diapers are being used in hospitals letters were sent to prominent institutions caring for babies in several of our large cities, asking for data on this subject. The result is rather meager.

In one babies' hospital diapers made of several thicknesses of gauze are used on the girl babies, and in two general hospitals with children's wards a paper diaper is used next to the skin, inside the regular cloth napkin. This also only applies to girl babies.

All others communicated with, except the three mentioned below, are using the old-fashioned cloth diaper on all babies, depending on boiling, steam sterilizing, etc., to prevent infection.

One babies' hospital and two general hospitals in their children's wards have for several years been using a single service diaper very successfully on all babies and young children. This diaper is composed of a specially prepared paper, cheap gauze, and absorbent cotton, and is the result of many experiments with various papers, etc. The paper used comes in sheets twenty inches square, and is folded triangularly to form four thicknesses. For the small sizes one sheet folded twice is necessary, and for the large sizes, two sheets folded once. A small square of absorbent cotton is placed on the paper, and the whole is covered by one thickness of gauze.

The average cost of this diaper, as used in a hospital treating from fifty to eighty babies ranging in age from a few days to 3 years, is one and a half cents. This compares very favorably with that of the cloth diaper, when the cost of laundering, sterilization and the original and renewal cost are taken into consideration. Many believe that any additional financial outlay is more than made up by the safety from infection, which makes for increased efficiency.

One great advantage of the single service diaper is found in the fact that it obviates the danger of the personal equation. Of course boiling for one or more minutes will destroy gonococci. When reliance has to be placed on laundresses to see that these conditions are observed the possibility of error becomes appreciable. The factor of expense is a real obstacle in many institutions, however, so that the committee has added to the recommendation the approved method of sterilization. We feel, however, that the use of the single service diaper, destroyed

at once in the small incinerator after being soiled, furnishes the ideal method.

"F. That repeated examinations of all girl patients for the presence of vaginitis be made during their stay in the hospital."

This recommendation was adopted after some discussion.

The committee desires to suggest the following modification:

That nurses be requested to make daily inspection of the vulva of each girl at the time of bathing, and to report immediately the presence of the slightest suggestion of a vaginal discharge.

Fifty-five members approved the original recommendation. Two approve only in suspected cases or in cases where discharge appears. Another thinks the decision should be left to the visiting physicians of each institution and that the recommendation therefore should be omitted. A fourth approves because of the latency of the infection in some cases, and the fact that in this latest phase the diplococcus may not be demonstrable except by repeated examinations. This unquestioned fact answers the objection of another member, who considered that one thorough examination on admission is sufficient. Two members call attention to the question of the age of the patients. One says "to older girls especially this (repeated examination) would be an indignity, and because they are institutional wards is no reason why they should not have the same respect for their feelings manifested as their more fortunate sisters."

The committee decided to suggest a modification of the recommendation partly on account of this question of offending the modesty of the older girls, and partly on account of the danger of infecting them by frequent repetition of taking smears.

We recommend, therefore, that nurses be especially cautioned to make a visual examination on every possible occasion. This will train the nurses to be observant and to be on guard, and will not in any way outrage the modesty of the patients.

We may emphasize at this point the difficulty of framing recommendations which will be generally applicable to all grades of hospitals. A careless technic in securing vaginal smears would be almost as deplorable as the introduction of an occasional case of latent vaginitis. We must not forget that the recommendations, to be of any real service, must be scaled down to the capacities of the mediocre, rather than idealized to the level of the best. The latter class of institution does not need advice.

"C. That low toilets be provided."

This recommendation was adopted.

The committee desires to suggest the following modification:

That low toilets be provided and equipped with seats embodying the principles of the U shape.

Naturally, no one objected to the original recommendation and the committee simply makes the addition in order to conform to the recommendation for schools.

"H. That tub baths be not used for the routine bathing of girls, but instead, spray bathing."

This recommendation was adopted after some discussion.

The committee desires to suggest the following modification:

That for routine purposes the spray be used in place of tub baths for the bathing of young girls, and that older girls be sponged in bed.

Fifty-five members approved of the original recommendation and another would include all children, boys and girls. Three think spray bathing should not be used unless infection be present, and two object to the recommendation as undesirable or unnecessary. Another approves and specifies that girls should be sponged in bed when facilities for spray bathing are lacking.

In answer to a questionnaire sent to the chief resident physicians of thirteen large children's hospitals nine replies were received. The questions and answers follow:

1. How are babies bathed?

In some institutions several methods are in vogue, the number of times each method is mentioned will be indicated:

Bathed in tub, usually portable, 5; sponged in bed 2; spray bathing on slab 2; sponge bathing on slab 1; sponge on heated table 1; sponge in nurse's lap before a fire 1.

2. How are the older girls bathed?

Tub 8; spray 2.

All the hospitals use tubs for bathing convalescents, while sponge baths in bed are used for those who are sick. One hospital uses both spray and tub, and but one uses spray bathing only.

3. If tubs are used, how are they disinfected?

Thorough scrubbing with soap and water 5; disinfecting solution, scrubbed and scalded 2; disinfecting solution and scrubbed 2.

Several specified that disinfection also is used in "precaution cases."

4. If bathing on slabs is used how are the slabs disinfected?

Of the three hospitals which use slabs, one relies on changing the pad or blanket after each child has used it. In another the slab is scrubbed in addition, and in a third a solution of chlorid of lime is used as a disinfectant before the scrubbing.

In view of the satisfaction which spray bathing on slabs has given in several hospitals, it seems rather remarkable that the method is not more generally used. The committee has very strong belief in the necessity for bathing girls in bed, when the spray bath is not feasible. The difficulty of thoroughly disinfecting tubs is too great, in our opinion, to warrant their routine use. This, of course, does not deny the benefits of tub baths in typhoid fever, etc., where they are especially indicated. Apparently this belief is not shared in by most of these institutions.

It might be well also to call attention to the danger inherent to certain types of plumbing. The bell-shaped water inlet, placed low in the tub, and the hidden plug in the outlet are dangerous forms, which render it almost impossible to secure thorough disinfection of inlet or outlet pipes.

"I. That the principles of aseptic nursing be most thoroughly taught and enforced."

This recommendation was adopted.

The committee desires to present the following modification:

That nurses receive special instruction as to the nature of vaginitis, the ease with which it is transmitted, the methods of preventing its spread and the necessity for rigid aseptic surgical technic in its handling and treatment.

Naturally, there was no objection to the original recommendation. One member believed that it is probably the most important point in the letter to hospitals, since, "if aseptic nursing is not only taught, but also enforced, all other efforts will be of little avail." The committee, therefore, believes that the more specific recommendation is desirable.

The head nurses of several large children's hospitals were interrogated with regard to the danger of night nurses spreading the infection of vaginitis, and the possible reasons for it; also the number of patients, day and night, which should be assigned to one nurse.

Three believed that night nurses are not an important factor in the spread of vaginitis in hospitals. Three believed that they are more or less important, chiefly on account of being hurried by the necessities of

their work or because they lack close supervision. Two believed that night nurses should never be required to care for patients with vaginitis unless they have plenty of time to observe the strictest precautions, and one always puts a special nurse to care for them by night as well as by day. Seven believe that lapses in aseptic nursing technic are much more frequent by night than by day and four do not believe this to be the case.

Two believe that by day the number of cases for each nurse should not exceed two, five believe that one to three is the correct proportion, and four prefer one to four. Apparently these figures refer to babies with an average proportion of sick ones.

For night nursing the opinions stand as follows:

One nurse to ten babies 6; one nurse to twelve babies 3; one nurse to fifteen babies 2.

"J. That special facilities for the dispensary treatment of gonococcus vaginitis be provided and that adequate instructions be given to mothers."

This recommendation was adopted after some discussion.

The committee desires to suggest the following modification:

That a dispensary with special facilities for the treatment of gonococcus vaginitis be provided.

All the members approved of the original recommendation, especially the clause concerning the instruction to mothers. Without their cooperation treatment is sure to be unsuccessful.

One member suggests that the gynecologic clinic is a very satisfactory place for such cases. If by "clinic" is meant the room, this may be a good substitute for a special room; many hospitals could not supply the latter. There would be a distinct objection to having the children treated during the regular gynecologic clinic hour. The chief difficulty in establishing a special clinic, however, will be to secure the services of a competent physician to take charge of it.

One member states that dispensary treatment in his experience has failed to produce any results. Possibly this may be due to failure to secure the provision made in the next recommendation.

"K. That nursing care and supervision be given in the home."

This recommendation was adopted.

The committee has no change in this recommendation to offer. As one member suggests, this involves the whole question of the home care of the sick. No one objected to the recommendation, however, and it

would seem to be a sine qua non of successful treatment of vaginitis. The hospitals which cannot furnish it should refer their cases to those that can.

This completes the list of the original recommendations to hospitals. The committee desires to make two additional recommendations.

L. That mothers be instructed as to the dangers of vaginitis, the manner in which it is transmitted, the best method of protecting other children and the necessity for prolonged observation.

The intent of this recommendation was barely indicated in Item "J" of the list presented last year, which received the Society's approval. It seems worthy of much greater emphasis, however, as the responsibility both for much of the spread of the contagion and for the real efficiency of the treatment falls on the mother, at last analysis.

M. That all cases of vaginitis under observation be voluntarily reported to the local health officer in states and cities in which no legal requirements are in force.

Objections might be made to this on the score of its legality. If the term vaginitis is used, however, without the qualifying word "gonococcus," there seems to be no reason why such a report could be actionable in any sense; while it would be an undoubted aid to the authorities in enabling them to locate foci of infection.

There are several other matters concerning the problem of vaginitis which the committee desires briefly to call attention to:

First, the question of the disinfection of the bed clothes, night gowns and mattresses.

From the replies received to a questionnaire sent to several of the leading hospitals in the country some interesting data are available.

Out of fifteen hospitals only three use what may be called adequate methods for sterilizing mattresses by heat. In one institution army blankets are used in place of mattresses, which are sterilized under steam pressure after contagious cases only. In another eighteen-ply felt is used, which is boiled after use by each patient. In a third the regulation steam mattress sterilizer is used after each patient. It may be said that a fourth is preparing to install a steam sterilizer for mattresses and clothing.

The remainder rely on spraying mattresses with a disinfectant and then airing and, when possible, sunning them; or exposing them to the fumes of formaldehyd for twelve hours.

Five hospitals routinely boil the bed and body clothing of all patients, eight rely on regulation laundry work.

After vaginitis, mattresses are sterilized by heat in only five hospitals, a sixth, as said, being about to install a sterilizer. The remainder use the methods described above.

Clothing after use in cases of vaginitis is sterilized by boiling, or steam under pressure, or by the fractional method of steam sterilization, in six institutions; another using the sterilizing washing machine. The remainder rely on fumigation or soaking in a disinfectant solution.

The comparatively small number of representative institutions which are equipped with modern mattress and clothing sterilizers is somewhat surprising.

Another point concerns the question of the moral degradation engendered by vulvovaginitis in girls.

In last year's questionnaire physicians were asked whether they believed that gonococcus vaginitis stimulates the practice of masturbation. About 40 per cent. of those who answered believed that it does, either because of the disease per se or because of the treatment. The head of the social service department of one of Philadelphia's largest hospitals has knowledge of a number of instances in which such was the case.

It has also been noted by careful observers that many of these patients are sexually precocious, and show an unusual lack of embarrassment during examination.

While many of these instances of moral degradation, which undoubtedly could be multiplied, cannot be laid entirely at the door of vaginitis or its treatment, but must be considered the inevitable consequences of vicious heredity and environment, it is also true that many others are to be reckoned with the problems which vaginitis presents, and are intimately associated with the question of treatment.

They form an additional and unanswerable argument for prevention as against cure, and in favor of the recommendations presented.

This leads us logically to the last matter to be discussed.

What further steps might be taken to extend the benefits which we trust these recommendations may bring about.

The principle of the hygienic toilet seat is so valuable that health officers should be empowered to require their installation in all public toilets, in hotels, railroad trains and stations, tenements, playgrounds, comfort stations, etc.

It would also seem desirable that maternity hospitals and day nurseries receive some suggestions similar, in part, to these to be sent to hospitals which treat children. In maternity hospitals especial care should be paid to discovering latent gonococcus infection in the expectant mothers.

In closing, the committee desires to express its appreciation of the aid which the members of the Society have furnished and our sincere thanks for the almost unanimous response to the request for criticism of the original resolutions.

We are indebted to health officers throughout the United States and also to many superintendents of schools and hospitals, physicians, nurses and social workers, not only for answering our questionnaires, but also for giving us many valuable suggestions.

EPIDEMIC VAGINITIS IN CHILDREN

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It has long been the opinion of clinicians that the clinical and bacteriologic methods ordinarily used for the differentiation of gonococcus from other forms of epidemic vaginitis have not been sufficiently perfected to make them absolutely reliable. The literature of this subject, including the report of the American Pediatric Society on vaginitis in childhood, which was made to this Society in 1915, indicates that the bacteriologic technic of this disease involved in the accurate diagnosis of gonococcus vaginitis must still further be improved and simplified before it can be absolutely relied on for the accurate diagnosis of epidemic vaginitis in institutional and private practice.

There is perhaps little doubt in the minds of pediatricians as well as bacteriologists that a very large percentage of these cases are due to the gonococcus; and there is also no question but that the bacteriologic tests as now made as aids in the diagnosis of gonococcus vaginitis are essential and are of the very greatest value, and that at the present time we must rely almost wholly on these tests in making our diagnosis of this condition; but the fact remains that the routine staining method for the gram-negative, intracellular, biscuit-shaped diplococcus, which is chiefly relied on in making the diagnosis of this disease, is not altogether satisfactory.

PREVALENCE OF EPIDEMIC VAGINITIS IN CHILDREN

Epidemic vaginitis is now recognized as one of the most prevalent infections in most of our large cities. This is especially true in hospitals and other institutions which care for female children. At the present time there are about seventy-five of these cases being cared for by the Cincinnati Hospital and the Children's Clinic, which is run in cooperation with this hospital. Under careful treatment and rigid quarantine regulations the number of these cases in the Cincinnati Hospital and clinic have very materially diminished during the past winter. It is a very significant fact that the vast majority of our new cases come from other institutions, such as orphan asylums and children's

homes, and that nearly all of these new cases occur in children under school age. My inference, therefore, is that the public schools of Cincinnati have very little, if anything, to do with the spread of this contagion.

The marked prevalence of this disease in most of our large cities, as well as its intractability to treatment and its defiance of ordinary quarantine regulations, is recognized as presenting one of the most difficult public health problems presented by any of the contagious diseases.

The collective report of the committee above referred to indicates that the disease is on the increase. We may therefore assume that epidemic vaginitis is a contagious disease very prevalent among female children in our large cities and that the means now in vogue for the cure of this disease and for preventing its spread are quite unsatisfactory.

During the long experience which I have had with this disease in Cincinnati there has never been an instance in which the disease was contracted by adults, although these cases are constantly under the care of female nurses. In the report of the committee above referred to "eighty-five physicians have never known of an instance in which a nurse was infected during a ward epidemic of vaginitis, ten physicians have seen such an occurrence." It appears from these facts, therefore, that while the disease is very contagious in childhood, adults are practically immune. No satisfactory explanation has been offered as to the immunity of adults from this disease.

TRANSMISSION OF CONTAGION IN CHILDREN

In children this disease is not in the ordinary sense a venereal disease, that is to say the manner of its transmission is not by sexual contact. The contagion is carried to the vagina of the child in some way other than in which gonorrhea is spread among adults.

The grouping of the various causes by which the disease may be spread among children is outlined in the report of the committee above referred to, as well as in the voluminous literature of this subject.

The cases due to sexual contact are practically negligible. Here we have another marked difference between gonococcus vaginitis in children and in adults. It is a very remarkable fact that a disease which in the adult is rarely transmitted in any other manner than by sexual contact should appear in children as a violent epidemic, spread in an

altogether different way. The explanation of the difference in the manner by which this disease is spread in children and in adults has not received a satisfactory explanation. That the adult is very susceptible to the gonococcus contagion is a well-known fact; that children are equally susceptible to this contagion is fully recognized, and yet the manner in which the disease is spread in the child and in the adult could not be more unlike than if they were entirely different contagions. Is the explanation of these facts to be sought in some unrecognized change in the organism or organisms producing the disease, or in some peculiar change in the susceptibility of the vaginal mucous membrane to this contagion at different ages in the life of the individual?

DURATION AND COURSE OF EPIDEMIC VAGINITIS UNDER TREATMENT

The report of the above committee as to the time required for a cure summarizes as follows: "Fifty-three of seventy-one physicians consider that the time varies from six weeks to six months. One believes that the cure comes only at puberty." That the absolute cure of this disease from a bacteriologic standpoint is a matter of great difficulty in a very large percentage of the cases is the opinion of a large number of competent observers. That the disease very commonly, if relapses are taken into consideration, continues for years, even under careful medical supervision, is attested by the literature of this disease.

Every institution which pursues the careful follow-up system of its discharged patients finds that a large percentage of apparently cured patients are subject to relapse. My desire here is simply to call attention to the intractability of these cases under careful methods of treatment and to the fact that many of them continue for years; yet notwithstanding the prevalence of this disease in childhood the disease practically disappears at puberty. There is no question in my mind but that there is a tendency to a spontaneous cure of this disease at this time of life.

In the report of the above committee only eleven out of ninety-six physicians were found who "had as adult patients those whom they had treated for vaginitis during childhood." When one considers the prevalence of this disease in young girls and its rarity in older girls, except when produced by sexual contact, one cannot but conclude that this disease in the vast majority of instances is self-limited. As a rule

it disappears as the child approaches puberty, under simple methods of home treatment, such as ordinary cleanliness and mild soothing applications applied to the external genitalia. To my mind there is no other explanation for the disappearance of this disease at puberty, for surely the results of our present methods of treatment do not justify us in believing that the sudden disappearance of this disease at this period in the life of the child is due to systematic medical treatment.

COMPLICATIONS AND SEQUELAE IN EPIDEMIC VAGINITIS IN CHILDREN

My own experience, as well as the literature of this disease, leads me to believe that complications and sequelae of epidemic vaginitis in children are much less common than gonococcus complications and sequelae in the adult. Since 1905, when I encountered and reported an epidemic of this disease in the Cincinnati Hospital, I have had a very large experience with this disease, and during these years I have observed but one possible gonococcus complication (arthritis) in all of the cases that have come under my observation. In the report of the committee above referred to, 39 per cent. of the physicians consulted "have seen more or less severe systemic complications." I believe, therefore, that complications and sequelae in epidemic vaginitis in children are vastly less common than are gonococcus complications in the gonorrhea of adults.

METHODS OF TREATMENT AND THEIR COMPARATIVE VALUE

In the wide experience which I have had with this disease since 1905, I have had an opportunity to try many methods of treatment which have been suggested, and I have been forced to the conclusion that the simpler methods of treatment, such as irrigating the infected parts once a day with two quarts of a normal saline solution, followed by the injection of two or three ounces of a 1 per cent. solution of nitrate of silver, are more efficacious than the more severe forms of treatment involving the direct application of strong astringents and antiseptics to the vaginal vault and neck of the uterus. There can be no question as to the advisability of local treatment in these cases; such treatment undoubtedly shortens the course of the disease and it is not improbable that one observer may get better results by reason of his superior technic with a certain line of treatment than other observers using the same treatment with perhaps less care and skill in the technic.

It is my belief that the intractability of these cases in hospital wards is largely due to reinfection. For this reason we have in the Cincinnati Hospital divided the vaginitis wards into four compartments. New cases are admitted into compartment one and there remain until the gram-negative diplococcus can no longer be found in the smears taken from just within the vagina. They are then transferred to compartment two and are technically known as first-negatives. There they remain under treatment for a week and if the smear from the vagina at the end of that time is negative they are transferred to compartment three, where the treatment is continued, and are there known as second-negatives. If at the end of a week a third negative smear is obtained they are transferred to compartment four and treatment is discontinued. Here they remain for a week or ten days and if at the end of that time the smears from their vaginas are still negative they are discharged to the institutions from which they came or into the care of the children's clinic, which continues to look after them for a number of weeks to insure their convalescence.

EVILS WHICH MAY RESULT FROM THE TREATMENT OF EPIDEMIC VAGINITIS

I have been much impressed with the idea that physicians have not given sufficient attention to the ill effects which may result from the long-continued local treatment in these cases. In the vaginitis wards of the Cincinnati Hospital my attention was recently called to the fact that a small percentage of the children in this ward were practicing masturbation, and an inquiry developed the fact that three older girls of school age, who had been in the ward for a long time, were teaching the new-comers all kinds of bad habits.

They were found to be imitating the physicians in making cultures by introducing instruments into the vaginas of the younger girls. It was therefore felt that it was absolutely necessary to isolate these older children in order to prevent the development of these bad habits in the younger ones.

It is a self-evident fact that more or less harm may result from the frequent handling of the genital organs of these young girls and this is especially true in cases in which the treatment must be continued over a long period of time. I here call attention to the ill effects which may result especially from severe and frequent treatment, not for the purpose of advocating the discontinuance of local treatment in these

cases, but for the purpose of noting the fact that bad as well as good results may follow such treatment.

I have also found that very serious social problems have developed in the treatment of these patients in their homes. At the present time there are forty-five of these patients in Cincinnati treated in their homes under the supervision of the children's clinic. These patients have been reported to the health authorities and are therefore not permitted to attend school. They are, I believe, practically the only cases which are reported to the health department in Cincinnati. Most of these children are of school age and many of them, by reason of the fact that they are excluded from the schools, are not only deprived of the educational advantages which the public school offers, but they spend a large portion of their time in the street under very unfavorable hygienic and moral conditions. Many of these children go on for months with little or no vaginal discharge and yet we may be unable for any length of time to obtain from them negative smears indicating that they are from a bacteriologic standpoint cured of this disease.

I have been appealed to many times as to the injustice which is being done these children and yet I have found no way of solving the problem. It is my belief that hundreds of these cases in every large city run a mild course and are unrecognized; these children go to school apparently without spreading the contagion, they have little or no treatment and yet after a time they spontaneously recover.

It can be seen from the outline which I have presented that the social and public health problems which this disease presents are very great and that our knowledge of the disease from the standpoint of diagnosis, quarantine and treatment is not sufficient to enable us to handle this question in a satisfactory manner.

In discussing the question of the handling of these cases by public health authorities, and whether or not epidemic vaginitis should be classed among the reportable diseases, let the physicians of this Society and of the country ask themselves whether, in the present state of our knowledge of this disease, they would be willing to report to the health authorities a case occurring in their own families, the diagnosis of which rested solely on the morphologic and staining characteristics of the organisms found; that is to say, on the fact that a gram-negative, intracellular, biscuit-shaped diplococcus was found. If the term gonorrheal or gonococcus vaginitis were for the present dropped from the literature, and the term epidemic vaginitis substituted (this name not

suggesting to the lay-mind a venereal disease), I think it would be much easier to handle these cases from a public health standpoint.

It appears to me very evident that until we are in a position to make vaginitis a reportable disease and enforce the ordinary health regulations which are used in other reportable diseases we are not justified in excluding these children from our public schools.

DISCUSSION

ON REPORT OF COMMITTEE ON VAGINITIS AND DR. RACHFORD'S PAPER

DR. RACHFORD: During the last year and a half, in the Cincinnati Hospital, we have had a good deal of experience in the treatment of vulvovaginitis. This ward is divided into four compartments. Patients are admitted to the first of these, and from that are discharged, on a negative report, to the second compartment, called the first negative. Here they are kept for one week and then on negative findings they are discharged into the third compartment, called the second negative. From this, after one week of treatment, they are discharged on negative findings into the fourth compartment, in which they remain for one week without treatment, and then on negative findings are discharged into the hands of the children's clinic, which is practically the outdoors Cincinnati Hospital, so far as the children's department is concerned. Every child discharged from that institution is discharged into the hands of the children's clinic, and the supervision of these children is continued.

I have in this way come in contact with some of the problems here represented, and we have found it practically impossible, in the present state of our knowledge, to handle this disease in Cincinnati as we handle other contagious diseases. The public health problem is a very, very great one, and one that should require very serious consideration before we recommend that this condition be made a reportable disease, especially under the name of gonococcus, or gonorrheal, vaginitis. We have had the greatest amount of trouble, especially on the part of institutions, because this condition in Cincinnati is very largely an institutional disease. The children come mostly from the orphan asylums and children's homes, and comparatively few from private houses. When these children have passed through the various compartments of the vaginitis ward and are discharged, it is impossible, because of the name "gonorrhea," to get these children back into the institutions from which they come. As a result, they remain under the care of the children's clinic for a long time. Many of these institutions are presided over by boards of directors composed largely of women, and the name "gonorrhea" in connection with this disease strikes terror to them. I have had to go before a number of these boards in our city and try to explain to them that gonococcus vaginitis, or vulvovaginitis, is a disease of children that is very different from the same disease in the adult. I have told them that vaginitis, like many other diseases, such as pneumonia and typhoid fever, for example, runs a very different course in the child and in the adult.

As I have said, the term "gonococcus vaginitis" has caused a great deal of trouble in our city. The only cases of this disease reported there are those sent from the Cincinnati Hospital into the care of the children's clinic. These children, by reason of the fact that they have been treated at the hospital and discharged uncured, have been taken by the clinic and cared for in their

homes. This is done by visiting nurses and physicians from the children's clinic; but of course most of these homes are not very suitable places for the treatment of this disease. We have tried to educate the mothers in these homes in the care of these children, and have in many cases turned over the treatment to them, yet there is a group of thirty children from 6 to 11 years of age kept out of school for a year or longer, who are running the streets and are under the very worst social and hygienic conditions. I have been appealed to by public workers in our city to try to remedy this condition and do something for this group of children thus isolated and prevented from going to school. They are the only ones whose cases are reported. The physicians in Cincinnati never think of reporting a case of vulvovaginitis in private practice.

DR. HOLT: I think that we all appreciate the enormous labor that the committee has expended on this report, and I consider it a valuable contribution to the subject. There are perhaps only two points about which there are wide differences of opinion among us, and I suggest that we confine our discussion to these. The first is the recommendation to health officers, "that children known to have gonococcus vaginitis be excluded from schools, and not readmitted until the receipt of a physician's certificate stating that he has examined the child once a week during a period of three weeks, and that there has been no discharge during this time."

The second is "that gonococcus infection be made a reportable disease."

Except for these two recommendations, I believe that the report should be adopted. I doubt the advisability of making a majority and minority report on the recommendations submitted to the committee, but I do not think that we can unanimously agree on the points I have mentioned.

I believe with Dr. Rachford that if these children are generally excluded from schools, and only readmitted under certain conditions, there will be a great deal of concealment of the disease, and that a stigma attached to certain groups of children will exist, when there may be others attending school with just as severe an infection, but which has not been reported. I think we are not yet ready to take the position that gonococcus vaginitis in children should be a reportable disease or that children suffering from it should be excluded from the public schools. If they are so excluded, it will be necessary to make some provision for their education, and this creates a situation that we are not prepared to meet at present. If these two paragraphs could be omitted, the rest of the report could be voted on, and these left for future consideration.

One additional recommendation might, perhaps, be made, namely, that gonococcus vaginitis in young girls should not be considered as a venereal disease.

DR. RACHFORD: I make a motion that the report be adopted along the lines suggested by Dr. Holt, leaving paragraphs B and G for future consideration. It is important that the society should use the term "vulvovaginitis" rather than that of "gonococcus vaginitis" in discussing this disease.

DR. HAMILL: I should like to ask Dr. Rachford what he calls pneumonia in the child.

DR. RACHFORD: Pneumonia.

DR. HAMILL: This being the case, I cannot see why we should not call this disease gonococcus vaginitis. Merely because the clinical manifestations of the disease differ in the child from those of the disease in the adult, why should we call it by another name, any more than we should call pneumonia in the child by another name? There are several different varieties of the

pneumococcus and all of them produce very mild symptoms. The lobar form of the disease in early life is relatively mild, but it is, nevertheless, pneumonia.

DR. ADAMS: What are you going to do with the boys? In the Children's Hospital here we have had seven cases in children under 10 years at one time, two boys and five girls, belonging to one family. The infection came from the father, who infected the mother, and these children, who were distributed in two beds with the parents, became infected. You have not provided for the boys in these recommendations, and I think that the question of segregation also shows discrimination. Are these recommendations to apply to private schools as well as to public? The infection spreads in one as well as in the other. We have to consider that point in adopting the report. We are now protesting about stating the disease in the District of Columbia, and I offered to go to jail rather than state, under the Harrison Law, the nature of the ailment for which I gave morphin. We had a conference with the authorities and told them that we would go to prison rather than say what the disease is. The danger of suit against the physician for branding a child as a menace to the community must be considered, not only by physicians, but also by institutions and by the lawyers when it comes to be a legal matter. I have discussed it with lawyers. If the law is made, you cannot fall back on that. Our statute protects the physician from disclosing confidential matters learned from his patient.

I am willing to adopt the recommendations with these two left out. I do not think we are prepared to report the disease. The authorities say that a reportable disease is secret, and that the information given is not revealed to any one. Well, it is handled by clerks. Of course these clerks are not at liberty to tell, but, nevertheless, whether the secret gets out or not depends on the individual clerk.

DR. HAMILL: As a member of this committee, I am willing to have one of these recommendations deferred for future consideration. So far as the recommendation that recognized cases of this disease be kept out of schools, I am strongly in favor of it. I have a very profound respect for this disease. I do not know whether in Philadelphia it is more prevalent than elsewhere, but it is one of the most perplexing problems we have to do with from the public health standpoint.

In discussing this subject I have several times asked a question which I should like to put to Dr. Rachford, namely, if you had a daughter and knew that there were cases of gonococcal vaginitis in the school she attended, would you keep her in the school? If children have recognized cases of the disease, they should be kept out of the schools, and if it is necessary to provide some way of educating them, the health departments should see to its being done. I realize that a certain stigma would be attached to children so treated, but in a case of this kind we must consider the effect, not on the infected individuals, but on the larger group with whom they come in contact.

Therefore, I am not willing to see the action on the recommendation to exclude recognized cases of vaginitis from schools deferred.

DR. CARPENTER: It seems to me that it is scarcely necessary to debate this point, since all the chief medical school inspectors who replied to the questionnaire sent by the committee stated that they are excluding all known cases of the disease from the schools. There does not seem to be any objection on the part of health officers to a regulation excluding children with vaginitis from school, and although there may be no law providing for the exclusion

of such children, the health officers practically do exclude them whenever discovered. I am also strongly in favor of our going on record as approving of the reporting of vaginitis, because it is now a reportable disease in ten states and because I believe that eventually in every state vaginitis will be a reportable disease. I could not subscribe to permitting a child with an active gonococcal discharge to attend school.

DR. FIFE: I want to call attention to the fact that Section G does not read, "Cases of gonococcus vaginitis" themselves, but "gonococcus infection" generally, in girls or boys.

DR. SMITH: I should like to ask a question regarding point B. What is the real object of excluding the children from school? If our desire is to limit the spread of the disease, we are not accomplishing that, but only reducing the number of cases in a particular school. By turning loose these children on the community they spread the disease more when running the streets than when in school. We are not making any real progress towards controlling the disease in the community by simply excluding the children from school. That is why I am opposed to this recommendation.

DR. CARR: With reference to the question of pneumonia. Pneumonia is reported, not as pneumococcic infection, but as pneumonia, and I see no reason why vulvovaginitis should not be so designated, and not as gonococcic vaginitis.

DR. HAMILL: Dr. Rachford spoke of gonococcus vaginitis in the adult and vulvovaginitis in the child.

DR. RACHFORD: Dr. Hamill misunderstood me. I did not mean to intimate that they are different diseases. I was cut short in the discussion, and did not get a chance fully to explain. I do not believe that they are different diseases, but that they are different manifestations of the same disease in the child and in the adult.

DR. FREEMAN: Is Dr. Rachford's motion seconded?

DR. HOLT: It was my motion.

DR. RACHFORD: I will second it.

DR. FREEMAN: It is moved and seconded that this report be adopted except paragraphs B and G, which are to be voted on later. All in favor will say "aye"; contrary, "no." The report is adopted, then, with these exceptions.

DR. HOLT: Can we take these paragraphs up separately? I move the adoption of paragraph G.

DR. FREEMAN: It has been moved and seconded that paragraph G be adopted.

DR. RACHFORD: I am opposed to making the disease reportable, because I have found in Cincinnati that in the present state of our knowledge this is not practicable. In the first place, our cases in Cincinnati almost all come from institutions, and not from schools. Cases in private practice are not reported. If a few children from an institution are excluded because they have gonococcic vaginitis, why should not this institution be quarantined and all its children excluded from school. Are you prepared to recommend that the children of all orphan asylums and other institutions in which the disease is prevalent should be excluded from our public schools? I believe that in the present state of our knowledge we are not prepared to act on this question.

DR. HOLT: I do not think that many cases come from schools, but that many do come from the homes of the children. In a single year we had sixty-

five infants who were already infected apply for admission to the Babies' Hospital. They had not been in schools. When the cases have been followed and the source of infection traced, the home has been found the most frequent origin of the disease. So far as young children are concerned, and my experience is chiefly with children under 3 years old, next to the home, infection has been traced to the day nursery. I move to adopt the recommendation in order to have it discussed.

DR. NICOLL: In the state of New York we are trying to have communicable diseases reported, and have lately made it a rule that when a physician is not in attendance the head of the family must report a communicable disease. If we introduce into the list of reportable diseases such a disease as this, it will make this rule a farce. The heads of families will not report the cases. I can promise you that this recommendation will not be carried into effect in the state of New York, outside of New York City, whatever action may be taken by this Society.

Another thing that I wish to call attention to is that gonococcus infection means more than what we are discussing. It includes ophthalmia neonatorum, for instance, which is a reportable disease in New York; but vulvovaginitis is not.

DR. VAN INGEN: It is a question whether this Society believes that gonococcus infection ought to be a reportable disease, and not whether any state health department can carry into effect a recommendation that it be made so. The question is whether we believe that it should or should not be reported.

DR. FREEMAN: I think that we had better have a standing vote. Those in favor of the motion to adopt paragraph G will kindly stand; those opposed. The motion is lost by a vote of eight to twenty-two.

Now there is paragraph B to dispose of.

DR. HOLT: I move that paragraph B be adopted, in order to bring the question before the house.

DR. FREEMAN: The question is open to discussion. Shall children with gonococcus vaginitis be excluded from the public schools and not readmitted until the receipt of a physician's certificate, stating that he has examined the child once a week during a period of three weeks and that there has been no discharge during this time? Is there any discussion on this question? If not, we will again have a standing vote. Those in favor of adopting this recommendation will kindly stand; those opposed. The motion is carried by one vote.

DR. HOLT: Don't you think that the character of the vote should be mentioned in the report?

DR. ADAMS: All present did not vote.

DR. HOLT: A majority of but one indicates that this is not the sense of the Society, and ought not to go on record as the recommendation of the Society.

DR. RACHFORD: The Society would be in an awkward position in recommending that the disease should not be considered reportable, and yet that children with it should be excluded from the schools.

DR. GITTINGS: We wrote to all the members of the Society, and their answers showed forty-seven for this and seventeen against it.

DR. HOLT: My point is that this is a letter to go to the health officers, and I think that in it we might state that the other recommendaions were adopted unanimously, and this one simply by a majority vote.

DR. GITTINGS: In framing this letter, we used the word "city," and I would move that the state health officers, as well as the city health officers, be included. (The motion was seconded and carried.)

DR. ADAMS: I move that the report as amended be adopted.

DR. HOLT: Would it be possible to have this amended further by stating that in regard to excluding children from the public schools, it was a majority vote only, and not a unanimous one?

DR. HAMILL: As a member of the committee, I wish to say that I should rather withdraw this recommendation altogether. The committee has given this matter long and most thorough consideration, having studied it for two years, and forty-seven members of the society replied that they were in favor of it. As the vote stands here, there were not seventeen men who voted against it. The vast majority of the members of the society are in favor of it, but as long as the vote was not unanimous, I believe that it would detract from the value of the general report to include it. I, therefore, make a motion that the report be adopted without that recommendation; although I think that in doing so you are omitting a most essential thing.

DR. GITTINGS: I would second Dr. Hamill's motion. As a matter of fact, exclusion is being done by health officers at present.

DR. FREEMAN: It has been moved and seconded that this paragraph be eliminated from the report.

DR. CARR: I would say that in answering the questions from the committee we answered them according to our individual views, perhaps in part without full consideration of the work of the committee, but on coming to the meeting and hearing the discussion in regard to the feasibility of putting such regulations into effect we have a right to change our views. This is no reflection on the work of the committee. We may personally object to having our children go to schools where there is gonococcic vaginitis, but we feel that in making the recommendation that children with this disease be excluded from the schools we should have something tangible to go on, and when we hear that at present these rules are not easily carried out, I believe that the decision to eliminate that paragraph is wise. If we cut these children off from school life, we must have more provision for their care than is afforded in paragraph B. It is, as I stated, no reflection on the committee, but simply a matter of fact that at this time the Society feels that it must not urge health officers to carry out these recommendations.

DR. COWIE: It seems to me that a gonococcus infection is often attended by more serious consequences than is a measles, scarlet fever or a smallpox infection; for that reason I think that if there is one disease which should be excluded from the schools it is a known gonococcus infection. I think we have no positive evidence that children do not become infected in the schools. I see no reason why this disease should not be reported to the state board of health. It seems to me that this is the only way in which we can gain a knowledge of its extent in the community. We have a law in Michigan which is supposed to compel physicians to report all venereal diseases to the board of health. It is true that this has not been complied with as thoroughly as it should be, and that some physicians are out of sympathy with it. We have had no trouble resulting from the report of these cases. The cases are reported by number and not by name. I do not see why we should not attempt to control this disease as thoroughly as we attempt to control scarlet fever,

measles or smallpox. I appreciate that as yet a suitable plan has not been worked out. If a physician has a patient with gonorrhea or gonorrheal infection under his care, I believe that he should exclude that patient from the schools: it requires only a little tact to do this without giving general publicity to the case.

DR. RACHFORD: I should like to ask how many members of this Society would be willing to report a case of this occurring in their own family in the present state of our bacteriologic knowledge.

DR. SMITH: Just a word as to the statement that the disease may come from the schools, made by Dr. Cowie. I think the fact that the greater number of cases come from other sources than the schools can be proved, and that in excluding children with this disease from the schools we are attacking a very small portion of the problem.

DR. COWIE: Pardon me for speaking again. I have seen so many children infected because of poor and improper isolation that I cannot help feeling quite keenly on the subject. I am sorry that I have not heard the committee's report or the discussion in full, having come in late. I think every effort possible should be made to control these infections.

DR. FREEMAN: The motion is that paragraph B be dropped from the report. All in favor of eliminating this paragraph will please stand up. Those opposed. There is quite a large majority in favor of the motion, so the paragraph will be dropped.

DR. ADAMS: Now I will move that the report as amended be adopted, as the recommendation of the Society. (The motion was seconded and carried.)

PROVOCATIVE AND PROPHYLACTIC VACCINATION IN THE VAGINITIS OF INFANTS*

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We have had to contend with the problem of vaginitis, just as so many others have had to do in similar institutions. It is not my intention to write a review of the trials and tribulations encountered during the five years since we have been housed in modern buildings and have made every effort to combat this insidious disease. As we have profited in some respects by experience, however, it seemed as if it might be of value to those who are actively interested in this problem to communicate briefly some of the lessons learned during this period.

Our endeavors have been directed in various directions: in preventing the admission of infected infants, in attempting in many different ways to avoid a spread of infection, in diagnosing cases at the earliest possible moment, and, finally, in resorting to every means to effect a cure. It should be realized at the outset, although the distinction is not always sharply drawn, that vaginitis presents a problem in a home or asylum for infants totally different from that which it presents in a hospital. In the latter the solution is comparatively simple, for all that is necessary in order to eradicate the disease is to cease admitting girl infants and to discharge those infected, one by one, as they are cured of the ailment for which they were admitted to the hospital. In the asylum, on the other hand, when a case of vaginitis slips past the admitting physician, or arises apparently de novo in one of its wards, it is realized that a heavy burden has fallen on the medical staff, for this infant will have to be guarded under quarantine for months or years, and will at all times constitute a threatening source of infection. We have had a variable degree of vaginitis; at times a lull, at others a sudden increase in numbers. At present, due to the regulations which are in force, the number of cases is comparatively few. It may be

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remarked, however, that during these years no instance of ophthalmia, of arthritis, or of infection of any of the personnel has occurred. There have been four instances of specific urethritis in boy infants, and one of rectal infection. This urethritis lasted but a few weeks and did not give rise to a positive complement fixation reaction, so that we believe it involved merely the anterior urethra.

The diagnosis of gonococcus vaginitis is not always easy to establish. In the first place, it is at times confused with other types of this disease, for there is no doubt that this inflammation may be due to micro-organisms other than the gonococcus. For months we harbored a case due to the streptococcus, which was present in almost pure culture in the vaginal discharge, and was furthermore identified on postmortem examination from cultures taken from the cervical canal. There was an absence of gonococci both during life and after death. These, however, are not the difficult instances we refer to, but the borderline cases, which are exceedingly puzzling, especially those showing merely pus cells on microscopic examination. If these cells are numerous, an inflammation is undoubtedly present, and in the great majority of cases the infecting organism will prove to be gonococcus. The specific nature of this infection is all the more probable if there are no micro-organisms to be seen in the field among the cells. One exception should be borne in mind as to the diagnostic significance of pus cells. This subject was called to our attention by noting many leukocytes in the smear of an infant only 48 hours old, who was brought to the institution for admission. It hardly seemed as if this were an instance of gonococcus vaginitis, although it is perfectly possible for an infant to be infected in this way during parturition, so we had some tests carried out in order to ascertain how often pus cells are encountered in smears taken from infants during the first two days of life. These tests were kindly carried out by Dr. Edwin Langrock. They showed that in about 50 per cent. of infants pus cells may be found in vaginal smears taken within the first forty-eight hours of life, so that it would seem that they must not be regarded as pathologic, but probably as the reaction of the external tissues to the inevitable invasion by bacteria. Possibly a similar inflammatory reaction occurs in the intestinal canal.[1] It should be understood that for these vaginal

1. In this connection it would seem of interest to note that leukocyte counts of new-born infants were found frequently to be high, the total per cubic centimeter reaching from 15,000 to 23,000, with a differential cell count presenting the adult type, namely, from 60 to 75 per cent. of polymorphonuclears.

smears, as well as all others referred to in this paper, an applicator tipped with moistened cotton was inserted deep into the vagina, so as to come in contact with the cervix.

As we inquire deeper into the cause of the spread of vaginitis, it would seem to resolve itself, in the last analysis, to a consideration of but one more phase of the general problem of the dangerous but healthy carrier. Although there can be no doubt that the disease is frequently communicated by means of clothing or utensils, the fundamental cause of the infection of one or more infants, in institutions where every care is exercised, must be considered the latent carrier, some healthy infant who harbors the gonococcus. Such has been our experience. For two years a pathologist devoted about two hours daily to the making of routine microscopic examinations of vaginal smears of the infants in the asylum. Wherever a case of vaginitis arose, the routine procedure was to make examinations three times during the following week on every infant in the ward in order to ferret out the source of the infection. A card catalogue was kept both of the individual infants and the various wards. Repeated tests brought to light some case in which, in spite of the absence of discharge, gonococci were evident in the smears. Recrudescences of infection occurred in one ward or another every few months and sometimes oftener. We are confronted, therefore, with a problem similar to that in typhoid or diphtheria, in which the carrier constitutes the main stumbling block in the path of prophylaxis. In the case of vaginitis the solution is rendered still more difficult in view of the heightened susceptibility of infants to infection.

During the past five years necropsies have been performed on four infants who had vaginitis while in the institution. (We are able to carry out postmortem examinations on fully 75 per cent. of the children who die.) This offered an exceptional opportunity to gain an insight into the pathologic changes of the common nonvirulent form of this infection. The pathology of this disease is generally glossed over in textbook descriptions. Furthermore, judging from the literature, we conclude the number of postmortem examinations of cases of this type is not large. We should expect this to be the case, as very few hospitals admit vaginitis, which must therefore constitute merely a chance pathologic condition met with in the course of some primary fatal disease. One of our cases had existed but three weeks, two patients were known to have had vaginitis for months, and one for a

year or more. They all showed the same pathologic condition, which may be summarized in a few lines: Macroscopically the vagina appeared negative, as did the body of the uterus and the appendages. The only abnormal condition was redness of the tip of the cervix, which, however, did not extend along the canal to the internal os. Microscopic examination confirmed the gross anatomic appearance of these structures. In every instance the entire vagina, the uterus and the tubes were removed for microscopic examination, which was kindly carried out by Drs. Eli Moschowitz and Alwin Pappenheimer, whom I take pleasure in thanking for their courtesy in this connection. The sole lesion was an inflammation of the cervix about the external os, a round-cell infiltration of the submucous tissues. Guided by these postmortem examinations, we must regard, it would seem, the average gonococcus infection as involving the cervix rather than the vagina, and must consider the infection a cervicitis rather than a vaginitis. It is in the cervix that the gonococcus finds a most favorable nidus. In a study published a few years ago from this service by Rubin and Leopold,[2] an inflammation of the cervix was frequently seen by direct examination. In the recent preliminary report of the vaginitis committee of the American Pediatric Society[3] it may be noted that eleven gynecologists who responded to their questionnaire thought that the cervix or uterus at times showed evidences of this disease. In the adults it has been reported that 95 per cent. of the chronic cases showed a cervicitis.[4] As the result of personal experience we must conclude that the vagina is comparatively immune in this infection, especially when the disease has reached the subacute or chronic stage.

There seems to exist a very general impression that vaginitis is more particularly a disease associated with child-caring institutions, and that infants brought up in the homes of the poor are infected far less frequently. This has not been our experience. During the year 1915 sixty-six infant girls were admitted to the institution and seventy-two rejected; of these seventy-two, sixty were refused admission on account of vaginitis, thus making the total infection noted in these children almost 50 per cent. It should be added that only three of the rejected patients were referred from other institutions, and that the remainder came direct from their homes. Further investigation may

2. Rubin, I. C., and Leopold, J. S.: AM. JOUR. DIS. CHILD., 1913, v, 58.
3. Tr. Am. Ped. Soc., 1915, xxvii, 331.
4. Menge, K.: Handbuch der Geschlechtskunde, Vienna, 1912, ii, 323.

possibly show that this ratio of positive cases is exceptionally high. As a result of having to refuse so many infant girls the institution now harbors one-third girls and two-thirds boys. It would be of theoretical as well as of great practical interest if we could know the results of a similar examination of older girls. From a limited experience of girls between the ages of 4 and 10 at the Tuberculosis Preventorium, I may state that not a few children of this age show signs of infection, although the danger of the spread of the disease seems to have become greatly lessened at this age.

One of the great difficulties in trying to combat vaginitis or cervicitis is that we find it impossible to recognize the infectious case in its earliest stage, in other words, the danger of the latent carrier. To overcome this difficulty we have made many attempts to convert the carrier into an open or florid case. Various drugs have been injected into the vagina in order to bring this about, but as they were found of no practical value, it would serve no purpose to enter into detail concerning efforts of this kind. For the past year, with this end in view, all infant girls have received three subcutaneous injections of gonococcus vaccine soon after they were admitted to the institution. These infants, it should be understood, had all shown an absence of pus cells on admission. The vaccine was prepared from a culture isolated from one of the cases in the institution, and 250, 500, and 750 millions were injected with three day intervals. The object of these vaccinations was to determine whether they would prove provocative and bring to light latent infections. In adults with urethritis it has been found by Asch[5] that injections of vaccine lead to a discharge containing pus cells and gonococci. The dosage which we used was entirely empirical. As a result of experience it would seem that it could be much smaller; indeed, at the present time we are giving only 100, 200 and 400 millions. Moreover, two injections may prove sufficient, as we have rarely brought about a discharge by means of a third inoculation. During the past year such provocative injections have led to the discovery of eight new cases during the first week or two following their admission (Table 1), and to the unprecedented result that not one case of vaginitis has slipped into the main institution from the admitting pavilion. We have made use of this diagnostic aid not only at the time of admission, but in order to discover carriers in dormitories, where sometimes sporadic cases of vaginitis arose (Table 2).

5. Asch, P.: München. med Wchnschr., 1915, No. 39.

TABLE 1.—ROUTINE PROVOCATIVE VACCINATIONS

Name	Age	Admitted	Date of Vaccination	Cervical Smear	Vaginal Discharge	Macroscopic Pus	Microscopic Pus	Gonococci	Remarks
M. G.	8 mo.	11/15/14	.....	11/15/14	—	—	—	—	Date of vaccination is always that of the first injection; two other injections were given at three day intervals
				12/12/14	—	+	+	—	
			4/27/15	4/25/15	+	+	+	—	
				5/ 1/15	+	+	+++	+	
				5/ 3/15	+	+	+++	+	
A. S.	11 mo.	4/15/15	.....	4/15/15	—	—	—	—	Smear after third injection loaded with gonococci; discovered in reception pavilion
				4/20/15	—	—	—	—	
			4/24/15	5/ 6/15	+	+	+	+	
				6/ 1/15	+	+	+	+	
				7/10/15	+	+	+	+	
				9/ 8/15	—	+	++	+	
H. B.	3 mo.	12/21/15	.....	12/21/15	—	—	—	—	Vaccine given a second time to discover latent infection in this ward
			2/ 2/16	2/ 9/16	—	—	—	—	
				2/25/16	—	—	++	—	
			3/ 1/16	3/16/16	—	+	++	—	
				3/29/16	—	+	++	+	
R. G.	11 mo.	12/14/14	.....	12/14/14	—	—	—	—	Vaccinated in order to find gonococci; a discharge resulted which lasted about a month and a half
				1/ 9/15	—	+	—	—	
				3/ 1/15	—	+	++	—	
			4/27/15	5/ 5/15	+	+	+	+	
				6/ 1/15	+	+	+	+	
E. S.	3 yr.	11/ 1/15	.....	11/ 1/15	—	—	—	—	Vaginal discharge incited, which lasted about three weeks
			11/21/15	11/29/15	+	+	+	+	
				12/16/15	+	+	+	+	
				3/ 7/16	—	—	—	—	
				3/10/16	—	+	+	+	
				4/11/16	—	+	+	—	
M. H.	3 yr.	7/13/15	.....	7/13/15	—	—	—	—	Vaginal discharge incited, which lasted about two weeks; discovered in reception pavilion
			7/15/15	7/29/15	+	+	+	+	
				8/ 3/15	—	±	+	+	
				8/ 9/15	—	—	—	—	
				3/10/16	—	+	+	—	
				4/14/16	—	—	+		

TABLE 2.—Provocative Vaccination in Old Cases of Vaginitis, Latent Carriers

Name	Date of Vaccination	Cervical Smear	Vaginal Discharge	Macroscopic Pus	Microscopic Pus	Gonococci	Remarks
S. L.	.....	1/15/14	+	+	+	—	Positive result after negative period of two years
		12/20/15	—	—	—	—	
		12/30/15	—	—	—	—	
	2/ 1/16	2/ 6/16	—	—	+++	—	
		2/ 9/16	—	—	++	+	
		4/20/16	—	—	+	—	
F G.	.....	11/ 8/14	—	+	—	—	No temperature reaction
		12/20/14	—	+	+	—	
		12/20/15	—	—	+	—	
		12/30/15	—	—	—	—	
	2/ 1/16	2/ 6/16	—	—	+	—	
		2/ 9/16	—	—	+	—	
		4/20/16	—	—	+++	++	
		5/ 7/16	—	—	+	—	
L. E.	.....	11/ 8/14	—	+	+	—	No temperature reaction
		12/20/14	—	+	++	—	
		12/20/15	—	—	+	—	
		12/30/15	—	—	+	—	
	2/ 1/16	2/ 6/16	—	—	++	—	
		2/ 9/16	—	—	+++	+	
		4/20/16	—	—	—	—	
G. S.	.....	11/10/14	—	+	+	+	
		12/ 8/14	—	+	++	—	
		1/20/15	—	+	+	—	
		12/15/15	—	—	—	—	
		12/30/15	—	—	—	—	
	2/ 1/16	2/ 6/16	—	—	+++	+	
		2/ 9/16	—	—	++	+	
		4/20/16	—	—	—	—	
F. G.	.....	6/ 8/14	+	+	+	+	
		12/15/14	—	+	+	—	
		1/12/15	+	+	+	—	
		12/20/15	—	—	—	—	
		12/30/15	—	—	++	—	
	2/ 1/16	2/ 6/16	—	—	++	—	
		2/ 9/16	—	—	++	+	
		4/20/16	—	—	+	+	

TABLE 2.—PROVOCATIVE VACCINATION IN OLD CASES OF VAGINITIS, LATENT CARRIERS—(*Continued*)

Name	Date of Vaccination	Cervical Smear	Vaginal Discharge	Macroscopic Pus	Microscopic Pus	Gonococci	Remarks
R. L.	.....	5/18/14	—	+	++	—	Went home in April
		12/20/14	—	+	+	—	
		12/18/15	—	—	—	—	
		12/30/15	—	—	—	—	
	2/ 1/16	2/ 8/16	—	—	++	—	
		2/ 9/16	—	—	++	+	
S. R.	.....	10/12/14	—	+	—	—	
		12/15/14	—	+	+++	—	
		1/18/15	+	+	+	—	
		12/20/15	—	—	—	—	
		12/30/15	—	—	+	—	
	2/ 1/16	2/ 6/16	—	—	++	—	
		2/ 9/16	—	—	++	+	
		4/20/16	—	—	++	+	
B. K.	.....	12/10/14	—	+	—	—	
		1/12/15	—	+	—	—	
		12/20/15	—	—	—	—	
		12/30/15	—	—	+	—	
	2/ 1/16	2/ 6/16	—	—	+	—	
		2/ 7/16	—	—	++	+	
		4/30/16	—	—	+	—	

For example, in one ward of twelve infants in which the girls had been free from vaginitis for a period of six to eighteen months, an active case suddenly developed, and although cervical smears failed to disclose its source, two carriers were brought to light by means of provocative inoculations. This has been the case on other occasions. This spring one case of vaginitis with gonococci and another showing pus cells, but no micro-organisms, was unexpectedly and unaccountably noted in the infirmary. There were six infant girls at the time in this ward. Provocative inoculation disclosed four positive cases after a second inoculation. Here was a veritable latent epidemic, which was uncloaked by means of the vaccine.

We are unable to state the exact scientific basis of the reaction fol-

lowing these inoculations. It is, however, not due to a rise of temperature. This was evident, as it occurred to a marked extent in some instances in which there was no febrile reaction whatsoever. It cannot be regarded as absolutely specific, for a positive result was brought about at times by similar injections of staphylococcus vaccine, although this was not found to be so reliable for this purpose as that made from the gonococcus. Indeed it is becoming more and more evident that many similar reactions of the tissues which we have been wont to regard as specific in nature, must be considered in large measure systemic cellular reactions. Whatever may prove to be its exact scientific basis, we firmly believe that it will be found of great practical aid in combating this difficult infection. The same principle might perhaps be applied to facilitate the recognition of carriers in other infections, for example, typhoid fever and pyelitis.

The vaccine was found to be of value not only as a diagnostic, but, to a certain extent, as a prophylactic measure. To this end we used it on about seventy-five infants and were able to change the entire nature of vaginitis in our institution. In patients who were vaccinated the vaginitis showed a mild type of infection. It is not to be expected that prophylactic injections can prevent the occurrence of carriers, just as diphtheria antitoxin cannot obviate the occurrence of diphtheria carriers, and typhoid vaccine cannot prevent the implantation of typhoid bacilli in the mucous membrane. However, the protected patients, instead of developing a vaginal discharge full of pus cells and gonococci, were found to have no discharge whatsoever, and to show as the only evidence of infection a few pus cells and microorganisms in the cervical smears. In other words, a nonclinical type of disease resulted. The bacteria frequently appear atypical under these conditions; they are degenerated and often very small, as has been described by many in connection with chronic cases. It is too early to state how long this partial immunity will last. We have not attempted to control its course by means of complement fixation, as our experience with this reaction has not been entirely satisfactory. For three years we made serum tests of this kind on the infants in the institution, in order to judge of the persistence of infection, but the results proved so contradictory that the attempt to solve the question by this means was abandoned.

There are some diseases which occasion not only a recrudescence of vaginitis, but seem to confer a susceptibility to infection. This is

especially true of scarlet fever. In this disease the susceptibility extends still farther, in that a systemic lack of resistance to the gonococcus results, so that joint infections and other evidences of a specific bacterial invasion result. Recently Nicoll[6] reported three cases of gonococcus arthritis in children from the scarlet fever pavilion of the Willard Parker Hospital, and others have been noted in these wards from time to time.

However, there is not merely an acquired susceptibility and probably also a natural susceptibility to gonococcus infection, but also a well defined natural immunity. This has been very evident in individual instances among the infants in the asylum. At times it has been very difficult to carry out an absolute isolation of vaginitis patients, more especially when some infectious disease has visited the institution. For example, about two years ago, during a considerable epidemic of whooping cough, it became necessary to isolate the children according to the presence of pertussis rather than according to vaginitis. Under such conditions it was observed that some infants did not develop vaginitis in spite of some months of exposure in these wards. In other words, these babies possessed a high degree of immunity (Table 3). Since then this idiosyncracy has been confirmed by further observations and there are at present five, or possibly six, infants in the institution who may be said to be immune, or almost immune, to this infection, and who during the past two years several times have chanced to be in wards in which vaginitis broke out and who nevertheless each time have escaped infection. These cases have been given provocative vaccination in order to make certain of their freedom from infection, but in every instance this has failed to incite any inflammatory reaction. We do not know whether this is to be considered a local or systemic immunity. We may, however, call attention to the fact that there seems to be no doubt that a similar immunity exists in the adult. It is to be remembered in this connection that there is frequently a difference in the configuration of the epithelium in different individuals. In some, the columnar epithelium begins outside of the cervix, in others the squamous epithelium, which is typical of the vagina, extends even into the cervical canal. These variations, as well as others relating to the number, the size, and the patency of the cervical glands, have been shown to be present in earliest infancy.[7]

6. Nicoll, M.: Arch. Pediat., 1914, xxxi, 804.
7. Moericke, R.: Ztschr. f. Geburtsh. u. Gynäk., 1882, vii, 84.

TABLE 3.—Cases of Natural Immunity *

Name	Admitted	Age on Admission	Cervical Smear	Vaginal Discharge	Macroscopic Pus	Microscopic Pus	Gonococci	Provocative Vaccination
P. K.	5/29/12	6 mo.	6/24/14	—	+	—	—	
			8/16/14	—	—	—	—	
			9/15/14	—	+	—	—	
			12/30/14	—	+	—	—	
			7/ 8/15	—	—	—	—	
			7/15/15	—	—	—	—	7/15/15
			7/20/15	—	—	—	—	
			3/ 7/16	—	—	—	—	
			5/ 4/16	—	—	—	—	
R. C.	5/23/13	2 yr.	5/24/14	—	+	—	—	
			5/26/14	—	—	—	—	
			6/24/14	—	+	+	—	
			1/ 5/15	—	—	—	—	
			5/14/15	—	+	—	—	
			7/ 9/15	—	+	+	—	7/15/15
			7/20/15	—	+	+	—	
			9/15/15	—	—	+	—	
			12/30/15	—	+	—	—	
			2/24/16	—	+	—	—	
			3/ 6/16	—	—	—	—	
N. S.	4/21/14	3 yr.	7/25/14	—	—	—	—	
			7/ 8/15	—	—	—	—	
			7/10/15	—	—	—	—	
			7/20/15	—	—	—	—	7/15/15
			9/ 7/15	—	—	+	—	
			12/30/15	—	+	—	—	
			2/ 6/16	—	+	++	—	
			3/ 4/16	—	—	+	—	
			5/ 4/16	—	—	+	—	
F. B.	6/16/12	2 yr.	6/24/14	—	+	—	—	
			7/10/15	—	—	—	—	7/15/15
			7/20/15	—	—	—	—	
			9/ 7/15	—	—	+	—	
			12/30/15	—	+	+	—	
			3/ 4/16	—	—	—	—	

* Unavoidably exposed for some months during spring of 1914, due to pertussis epidemic.

As is well known, the gonococcus has a particular affinity for surfaces covered with columnar epithelium, and is not able to attack those lined with squamous cells. This immunity is rare. In many instances it is probably not absolute and sooner or later, in the course of months, it will be found that infection takes place. It is reported as an observation of interest, rather than as one which can play a rôle in the epidemiology of this disease.

CONCLUSIONS

Postmortem examinations show that in the subacute and chronic cases of vaginitis in infants the cervix is most frequently involved and that the vagina generally shows no signs of inflammation. Cervicitis would therefore seem to be a more correct term, in this connection, than vaginitis.

Where numerous pus cells without bacteria are found in smears made from the cervix, an inflammation may be assumed to be present, and in the overwhelming majority of instances the inciting factor will be found to be the gonococcus. Other micro-organisms may, however, be the cause of the inflammatory process, for example a streptococcus, as in a case which was studied both during life and after death. It should be borne in mind that smears taken from new-born infants very frequently show pus cells, probably due to the invasion of the vagina by saprophytic bacteria, and that, in the new-born, they should not be considered pathologic or as evidence of gonococcal inflammation.

Gonorrheal vaginitis, or cervicitis, should not be regarded as a disease encountered especially in institutions, as it may be found in a considerable proportion of infants living in the crowded tenements in the city.

In child-caring institutions the greatest obstacle to limiting and controlling the spread of this disease is the difficulty of recognizing latent cases. It affords, therefore, but one more aspect of the problem of the healthy but dangerous carrier, and of the difficulty of devising methods to prevent contact infection. By means of provocative inoculations of gonococcus vaccine we have found it possible to convert the concealed carrier into an open case, and in this way to discover many cases which had eluded detection. Vaccinations have also some prophylactic value, and may either confer protection or render subsequent infection of a mild character, so that it assumes a bacteriologic rather than a clinical type.

There is not only a natural susceptibility to this infection and an acquired susceptibility, as occurs in the course of scarlet fever, but a natural immunity, which may be sufficient to protect infants who come in contact with infected patients.

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DISCUSSION

Dr. Talbot: I should like to ask Dr. Hess how long, after he has induced a discharge by provocative inoculation, the discharge persists, and whether it is accompanied with any extraordinary symptoms.

Dr. Sedgwick: I do not think I need say that we all appreciate this paper, which is very instructive. In a case in a private room of the private hospital at Minneapolis this winter, one of the students, a good one, reported that the child had gonococcus infection. Dr. Roddo, my colleague, looked at the patient, and was in doubt about the nature of the condition. We had the discharges studied by Dr. Larson of the university, and he reported that it was a pure proteus infection.

Dr. Hess: In answering Dr. Talbot's question regarding the persistence of the discharge, I would say that the time is variable. In some cases it persists for only a very short time, about two weeks. In others it persists for two months.

As Dr. Sedgwick has said, these cases are not all due to the gonococcus. I described in my paper a case due to the streptococcus, with necropsy, and we have had others in which no gonococci could be found. I hope that in view of the practical interest of the question, the members of the Society will make use of this method of prophylactic or provocative inoculation, and find out for themselves its diagnostic value.

SOME EARLY SYMPTOMS SUGGESTING PROTEIN SENSITIZATION IN INFANCY*

B. RAYMOND HOOBLER, A.M., M.D.
DETROIT

Through the painstaking researches of a great number of workers, we have come into possession of much information concerning the action of foreign protein when injected into animals subcutaneously, intraperitoneally or intravenously. The forms of protein most carefully studied are those of the various serums and the incentive for this study had its origin in the revolutionary discoveries of von Behring, Ehrlich, Wassermann, Abderhalden, Wright, Vaughan and a host of other workers. The study of the protein of the various serums led naturally to the study of the protein of the common food products, and out of this has come a great mass of information concerning the protein of milk, egg, meat and cereals. The leaders in the researches are Besredka, Vaughan, Osborn, Anderson and many others. Out of the tremendous amount of work which has been done in an effort to explain the phenomenon of anaphylaxis there have accumulated many facts which seem to be of such importance that they should be transported from the realm of the laboratory and made to serve the clinician in his daily work.

Two members of our society stand out pre-eminently in their efforts to bring to practical use the findings of the laboratory. Dr. Talbot[1] has shown the causal relation between egg protein and asthma; Dr. Schloss[2] has made clear through his researches that certain forms of infantile eczema are related to protein. It was thought for a long time that protein in order to enter the blood stream or body tissues unaltered must be introduced through the skin (subcutaneously, intraperitoneally, intramuscularly) or intravenously, but researches have been so abundant and conclusive during the past few years as to leave us no longer in doubt that a foreign protein, even when taken by mouth, may escape digestion and some of it be absorbed into the blood stream unaltered.

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* From the Children's Free Hospital of Detroit.

1. Talbot, F. B.: Boston Med. and Surg. Jour., clxxi, 695.
2. Schloss, O. M.: Am. Jour. Dis. Child., 1912, iii, 341.

The pioneers in this work were Ganghofer and Langer,[3] Lawatschek,[4] Ascell,[5] Moro,[6] Rosenau and Anderson[7] and Lust.[8] The latest and most convincing researches have just been published by Schloss and Worthen.[9] These workers have demonstrated beyond a question that absorption of protein occurs through the alimentary tract, particularly in those exhibiting signs of nutritional or gastro-enteric disorders. They state: "In gastro-enteric disorders, the mucous membrane becomes permeable, the degree of permeability being in direct ratio, apparently, to the severity of the disorder." My own researches in support of the proof of the absorption of milk protein into the blood stream unaltered are based on anaphylactic reactions in guinea-pigs.

The technic followed was that advised by Vaughan. Blood was collected from infants and children one hour after a feeding which contained milk protein in the usual quantity fed children of such ages. The blood was collected in citrate solution and taken to the laboratory and from 3 to 5 c.c. were injected intraperitoneally into normal guinea-pigs weighing about 250 gm. After suitable time had elapsed (at least 11 days), an injection of 5 c.c. of milk was also made intraperitoneally.

Blood was taken from normal children as well as from those with eczema, malnutrition and acute infections. The work, though still incompleted, confirms the work just published by Schloss and Worthen. Patients with eczema and malnutrition show undoubted permeability of the alimentary tract by positive anaphylaxis tests in guinea-pigs.

Just what happens when the foreign protein is absorbed unaltered into the blood stream has been the subject of numerous researches and much discussion without unanimity, but all are agreed that the individual absorbing such protein behaves differently under certain conditions than an individual who has not received this unaltered protein into its body tissue. This change in behavior toward the foreign protein by the individual is characterized as sensitization, or allergy.

The symptoms caused by the action of body tissue and fluids on this foreign protein is of great interest, for it varies from the mildest

3. Ganghofer and Langer: München. med. Wchnschr., 1904, li, 1497.
4. Lawatschek: Prag. Med. Wchnschr., 1914, xxxix, 185.
5. Ascoll: München. med. Wchnschr., 1902, xlix, 398.
6. Moro, E.: München. med. Wchnschr., 1906, liii, 214.
7. Rosenau and Anderson: Bull. Hyg. Lab., U.S.P.H.S., 1908, No. 45.
8. Lust: Jahrb. f. Kinderh., 1913, lxxvii, 244.
9. Schloss and Worthen: Am. Jour. Dis. Child., 1911, ii, 342.

disturbance to an explosion of such severity as to cause sudden death. A condition fraught with such far reaching consequences should command our best thought. It is therefore my purpose to attempt to collect some of the earliest signs and symptoms which are evident in the individual thus sensitized. In attempting to determine these symptoms I have studied the symptomatology of a large number of authentic sensitization cases reported in literature. I have also made extremely careful observations continuing from the time of birth on a considerable number of infants, who have later shown unmistakable signs of sensitization. Also, through the intelligent cooperation of mothers, I have collected a great deal of material concerning the early symptoms of protein sensitization.

A study of the symptomatology of acute anaphylaxis lays for us the groundwork of our suggested early symptomatology of "suppressed anaphylaxis." It might be well to get the picture of anaphylaxis both in guinea-pig and in man as described by Vaughan:[10]

> When a sensitized guinea-pig receives a reinjection of the same protein to which it has been sensitized after a proper interval of time, certain characteristic and practically invariable symptoms develop in three stages. The first stage is that of peripheral irritation. The animal is excited and evidently itches intensely, as is shown by its attempts to scratch every part of its body that can be reached with its feet. The second stage is one of partial paralysis. The animal lies upon its side or belly, with rapid, shallow, difficult breathing. It is disinclined to move, and when urged to do so shows more or less incoordination of movement, and muscular weakness, with partial paralysis, especially observable in the posterior extremities, which it drags. Rarely the animal dies in this stage. The third, or convulsive stage, begins with throwing the head back at short intervals. The convulsions become general, more frequent and violent, and the animal, having reached this stage, usually dies in a convulsion or immediately following one. Expulsion of urine and feces is frequent in the convulsive stage. Recovery after reaching the convulsive stage is exceedingly rare. When this stage is not reached, recovery usually occurs, and is so prompt and complete that after a few hours, or at most by the next day, the animal cannot be distinguished from its perfectly healthy fellows.
>
> When the hemologous protein is injected into a man sensitized by disease or by previous treatments, symptoms develop promptly, often within a few minutes, usually within a few hours. The stage of peripheral irritation is characterized by the sudden appearance of a rash. The rashes that occur most promptly are urticarial or erythematous. The lips and tongue seem swollen, and often the backs of the hands are swollen. The individual becomes apprehensive, says that he cannot breathe, and falls into a state of more or less marked collapse. In extreme instances there is retching, and occasionally vomiting. The second stage, that of great muscular weakness, continues for a variable time and usually rapidly passes away. In rare instances speedy death results.

10. Vaughan: Protein Split Products in Relation to Immunity and Disease, 1913, p. 245.

It will be seen that the symptoms of acute anaphylaxis in both animal and man may be divided into three groups: those relating to (1) the skin, those relating to (2) the upper and lower respiratory tract, and those relating to (3) the digestive system. The condition the symptoms of which we are attempting to give does not derive its impetus from a large quantity of foreign protein suddenly injected into the body tissue, as takes place in the production of acute anaphylaxis, but rather from the absorption of very small quantities every three or four hours, dependent on the interval of feeding. Naturally this slow and oft-repeated method of receiving the protein removes from the symptomatology the explosive character of the onset, but nevertheless the essential element, namely, the introduction of a foreign protein into the body tissues, should cause essentially the same symptoms, although such milder in form. Particularly is this true if we believe with Vaughan that the symptoms characterizing both acute and suppressed anaphylaxis are due to one and the same cause and differ only intensity of reaction. Vaughan maintains that in the process of digestion of the protein parenterally the poisonous portion of the protein molecule is set free within the body tissues, and there being no well established protective mechanism, the symptoms of acute or suppressed anaphylaxis take place, dependent upon the quantity and the rapidity with which the poison is set free. Vaughan further states that daily injections of a protein tend to suppress the explosive character of anaphylaxis. This would be analogous to an infant who, being fed daily on milk, absorbed a small quantity of it into the blood stream, unaltered by reason of the permeability of the intestine.

When sufficient quantity of protein is absorbed unaltered, then sensitization takes place and later reaction occurs, not in the explosive character of acute anaphylaxis, but rather in the form of the symptoms of suppressed anaphylaxis; the early evidences of which divide themselves into five definite groups: (1) those relating to the skin; (2) those having to do with upper respiratory tract; (3) those involving the lower respiratory tract; (4) those connected with the digestive organs, and (5) those referred to the nervous mechanism. In addition to this group of symptoms, there is the important condition of family predisposition toward one or another form of protein. In a large percentage of cases under my personal observation it has been possible to learn of some form of sensitization in father, mother or grand parents. It usually shows as hay fever, rose colds, asthma, or distinct reaction to

one or another form of food proteins, either egg, bean, oatmeal, milk, beef, fish. It is therefore of very great importance in our study of each case to determine whether or not we have to deal with an offspring whose parents have exhibited definite signs of sensitization.

Let us now consider the symptoms arranged according to the groupings just named. Perhaps the earliest manifestations of sensitization appear in the form of the various lesions of the skin. These may differ greatly in form and intensity. There may be the mildest erythema, either localized or general, or it may take the form of blotchy areas, often of very intense color. There may be urticaria, which may consist of a single wheal or be of the giant type or any degree between these forms. Usually the earliest forms are single urticarial wheals and are often considered by the mother the result of insect bites. There may be rashes, which are usually of the miliary type, and are found particularly about the neck and chest. This form is often thought to be due to dressing the infant too warmly. In addition to these forms, there may be a mere roughening of the skin, without exposure, similar to chapping.

The whole group of skin lesions due to sensitizations have usually been classified as intestinal rashes. Empirically, they have been associated with food disturbances, but just how they have been brought about has been an open question. Indeed, even with our advanced knowledge, it is difficult to explain the mechanism.

The next common phenomena of sensitization are those connected with the upper air passages. They manifest themselves in diverse ways. There may be symptoms which originate from vasomotor disturbances in the mucosa of the upper air tract. These exhibit themselves in (*a*) sneezing, (*b*) snuffles, and (*c*) rubbing the nose.

Sneezing is often a persistent symptom, until the mother is thoroughly alarmed, believing that the baby is catching a cold. This, coupled with snuffles, which may be so severe that the baby may be forced to breathe through its mouth, constitutes what has been aptly called by mothers a "dry cold." Infants who have been subject to many colds, yet never show a discharge or any other pathologic lesion other than perhaps a rather turgid nasal mucosa, are, in most cases, manifesting one of the common early symptoms of protein sensitization. Rubbing the nose is quite a familiar activity of certain infants and compares with that symptom noted commonly in animals as one of the early accompaniments of anaphylaxis.

The symptoms relating to the respiratory tract are usually of much later occurrence than those of the upper air tract. They are (*a*) wheezing, (*b*) periods of increased respiration, and (*c*) cough.

Wheezing is a very outstanding symptom, and one which can be readily detected. The expressions that mothers often use are that the child "breathes heavily" or that it "wheezes in its chest." This, in some of my cases, has been a very early symptom and precedes the true asthmatic attack by months. When one listens to one of these wheezing chests he is disappointed in finding so few variations from normal. The changes consist chiefly in increased breath sounds with a prolonging of the expiratory portion. The symptom of increased respiration is at first without dyspnea, but later with some dyspnea. These appear quite a time before the true asthmatic attack occurs. A cough occurs in some children, simulating that of mothers' croup, for which there is no adequate pathologic explanation. The cough is often very persistent, but usually is of short duration and disappears as suddenly as it comes on.

The symptoms relating to the digestive system often appear in the presensitization period and consist of an acute digestive disturbance. This is followed later by occasional vomiting attacks, in which an entire feeding may be ejected suddenly without any apparent cause. This vomiting is often accompanied by one or two urticarial wheals or by some one of the numerous skin manifestations.

The symptoms arising from some disturbance of the nervous system include the conditions generally described under the words irritable, restlessness, fretful and sleepless. Peripheral nerve irritability is very marked. It is most exasperating to watch an animal entering on an anaphylactic shock as it attempts to respond to the call of peripheral nerve endings. Something akin to this no doubt is experienced by an infant and produces for the time being periods of irritability, restlessness, and fretfulness. Sleeplessness is a rather frequent accompaniment of sensitization. Among several of my cases this was the outstanding characteristic and was the condition for the alleviation of which I was consulted.

General Characteristic of Symptoms: All of the above symptoms come and go with great rapidity. Not all of them occur together; often but one of them occurs and quickly disappears. Later on in the same child there is a different manifestation. As the sensitization becomes more marked, the symptoms increase in severity as well as in variety.

If the food protein is constantly increased, as is usual in bottle-fed infants, the manifestations of sensitization appear more frequently, remain longer and are more intense; thus many transient erythemas and fine rashes become displaced by the more permanent eczema, which appears first only in a few spots, as on the cheeks, over the fontanel, and behind the ears. If protein is persistently increased, the eczema gradually spreads until the entire body surface may become involved.

In like manner the respiratory symptoms become more prominent. The wheezing is more marked, the breathing more labored and eventually the extreme manifestation appears in the form of an attack of asthma. It rather frequently happens that the extremes of both the skin and the respiratory manifestations occur in one and the same patient, in which case we have a child with severe eczema suffering from frequent attacks of asthma. The other symptom groups tend to become more manifest and the finished product of protein sensitization present a distressing picture. Fortunately, all the symptom groups do not tend to appear in the same child. Certain children appear to be more susceptible to the skin manifestations, while others will show only the upper air tract symptoms, while in others the respiratory symptoms predominate.

I have mentioned only those symptoms which occur early in the period of sensitization. Some of these symptoms persist throughout the lifetime of the individual. Others disappear in the early years of life.

The process by which one becomes immune is little understood, although it has been possible to produce immunity, as demonstrated by both Talbot and Schloss. The relation of protein sensitization to various nutritional disturbances has been referred to by Schloss and Worthen. In their summary they state that their "results demonstrate the possibility that certain nutritional disorders in artificially fed infants may be due to the biologic character of the food." This line of research is well worth continuing, since it has already been shown by Vaughan that marasmus is one of the terminal symptoms of suppressed anaphylaxis in rabbits which have received daily injections of a foreign protein.

I am well aware that many of the symptoms named are symptoms of other very common diseases, and it is not my desire to claim that they occur only as symptoms of protein sensitization; but it is my observation that when the group of symptoms as outlined occurs and

reoccurs in an infant early in its existence, one should be on guard and should carefully watch for further developments.

Various tests may assist in diagnosis (*a*) blood examination for eosinophilia, (*b*) cutaneous skin reactions, (*c*) precipitin tests on urine, and (*d*) anaphylactic reactions. It is extremely important that this condition be recognized early, and when so recognized it need not go on to its extreme manifestation in the forms of eczema, asthma, malnutrition and, I have no doubt, many other nutritional disorders whose relation to protein sensitization have not yet been proved.

SUMMARY

1. I believe that permeability of the alimentary tract to unaltered protein in certain infants has been fully demonstrated.

2. The absorption of this unaltered protein produces a group of symptoms, mild at first, and later increasing in intensity, which I believe to be an expression of "suppressed anaphylaxis."

3. By early recognition of such cases, followed by proper food modifications, the symptoms may entirely disappear or be greatly ameliorated.

DISCUSSION

DR. SCHLOSS: The paper by Dr. Hoobler is extremely suggestive, inasmuch as he attempts to put in this classification a number of the milder manifestations. It seems only rational to believe that if we see the acute, explosive type of food idiosyncrasy, there must be milder attacks, in which the definite relationship to food is not so marked. The difficulty lies in obtaining conclusive evidence. There are many of these milder disturbances that may suggest themselves as due to food protein, and yet no definite evidence of the fact can be obtained. I have made a large number of skin tests in infants with chronic nutritional disorders, with inconclusive results. I have tried passively to sensitize animals with the blood of such infants, with similar negative results. This does not disprove the possibility that a number of these respiratory and skin disturbances may be of allergic origin, because the passage of sensitization from human beings to animals is not always sure, a high degree of sensitization being necessary for this to occur. There are certain types of food idiosyncrasies that do not give a positive skin reaction. It has been demonstrated in many instances that biologically precipitable protein may occur in the blood stream after the ingestion of certain protein foods, and that this is excreted in the urine. What becomes of this unaltered protein that is absorbed, and what is its effect on the organism, is questionable. While it has been definitely proved that in animals an absorption through the intestinal tract of unaltered protein does lead to sensitization, that has not been demonstrated to occur in human beings. This is a matter for actual demonstration.

The question of heredity is one of great interest, and it is quite true that in a vast majority of the cases reported and in most of those that I have seen,

there has been a decided family history. Often two or three of the family, parents and children, have been affected with some allergic condition. This probably explains the idiosyncrasies of some children to foods that they have never ingested. There are infants who exhibit symptoms the first time that they ingest a particular food, so there must be some state of the tissues, either inherited or acquired, that is different from the definite sensitization of an animal by a foreign protein.

The question of asthma is one that I have investigated. The results of the investigation were disappointing. They have not excluded the possibility that many of the cases were due to a food substance, but no definite evidence was forthcoming. The only thing to do is to leave the question open in cases of that kind. There were four cases of asthma that had a definite relation to food. Three were from the ingestion of egg and one from milk. In all desensitization was accomplished with good results. The children were free from asthma as long as they were kept desensitized.

DR. TALBOT: It should be remembered, in discussing this problem, that the condition of anaphylaxis which gives symptoms of asthma is a relatively rare condition. In looking through the hospital records I find relatively few cases of asthma. Skin cases which might be of anaphylactic origin are more frequent. Dr. Hoobler has referred to symptoms that are interesting, it seems to me, and some of them suggestive. I do not, however, agree with him about all of them. I have not been able to find any connection in the cases that I have studied between mild erythema and anaphylaxis. The mild erythema has been due to external irritation. In cases of urticaria I believe that the symptoms are all due to some form of anaphylaxis. Miliary rashes I have been unable to connect with any anaphylactic phenomena and I believe that they are usually due to inefficient excretion of the glands of the skin. The symptom of rough skin I think might in some instances be connected with anaphylaxis. In one of my cases it seemed to have a definite connection with this, but it may also be connected with deficient thyroid secretion.

There are two forms of eczema, one of which apparently has no connection with anaphylaxis, and is cured by merely reducing the fat in the food. In the other Dr. Schloss and others found positive skin tests. We believe that these cases are of anaphylactic origin, but the patients do not always get well when we remove the food that gives the skin test.

Of the respiratory symptoms, I think that sneezing in infancy is rarely due to anaphylaxis, but is due to a commencing cold in the head. Snuffles I would attribute to adenoids. Rubbing the nose, they used to tell me, was due to worms. Of the symptoms connected with the respiratory system, I think that wheezing, when there are râles in the chest, with no fever and nothing else to explain it, is of anaphylactic origin; but I do not think that wheezing is the principal thing on which to base a diagnosis. The diagnosis is made when the typical râles of chronic bronchitis are found, and, coincidently with these, we should have a prolonged expiration.

Then there is the symptom of croup, which I believe in most instances is not anaphylactic, but in a few instances results from ingestion of some food. I have three patients under my charge who can bring on an attack of croup at any time by taking raw or soft-cooked egg. On the other hand, we must not forget that the symptoms of croup as described by the parents might be laryngeal diphtheria.

There is no question, from the histories that we obtained, that some digestive symptoms are of anaphylactic origin, but I think that this is going to be one

of the last symptoms of anaphylaxis that we shall prove. Several of my patients have given of their own accord very long histories of anaphylaxis, and have described the following symptoms after taking protein: Some said that it stung them when they swallowed, and others that it made them have a "shivery feeling." I did not pay particular attention to this until the third child spoke of this "shivery feeling." The symptom of restlessness, in my experience, has been usually due to too many visitors and too much grandparents. In one family which gives a very pronounced history of anaphylaxis on the father's side, the older child had colic all through her infancy, no matter what food I gave her. It was an unexplained colic. The stools were all perfectly digested.

DR. HOOBLER: I wish to thank the two gentlemen for discussing the paper so thoroughly, and to say that I tried to make it very clear that I do not ascribe all the symptoms to anaphylaxis, but believe that they may occur in other conditions.

THE CALCIUM METABOLISM IN A CASE OF HEMOPHILIA *

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C. E., 9 years old, entered the hospital because of sudden enlargement of the right knee. He gave a history of repeated attacks of purpura, at times associated with vomiting and fever. The coagulation time of the blood was found to be two and one-half hours. Shortly after entrance he had a marked attack of purpura, with vomiting and fever; and during his stay in the hospital he had many spontaneous and subcutaneous hemorrhages. His brother, aged 19, was also under observation during part of this time for spontaneous hemorrhage into one knee.

A history of bleeding was obtained as follows: Of this family of twelve children, six girls and six boys, three of the boys were bleeders, one dying in infancy from hemorrhage. The maternal grandmother was a bleeder, and was one of ten children, four girls and six boys, three of whom were bleeders, herself and two brothers. The maternal great grandmother and her brother were the only bleeders in a family of seven children, five girls and two boys; her father (patient's great great grandfather) was a bleeder. Of the patient's family, in the order of birth, the third, fourth and eleventh male children were bleeders, the patient being the eleventh.

These data establish the case from the clinical side as one of hemophilia, with the characteristic transmission coming from the female side through two generations.

The coagulation time was determined by taking 3 c.c. of blood directly from a vein into a 10 c.c. test tube. It was placed in the incubator at 37 C. and carefully examined from time to time until the first definite appearance of clotting was observed (see table). During the control period the average coagulation time was two and one-half hours; during the third and fourth day of the calcium feeding period the coagulation time was lengthened two hours. The calcium content of the blood was increased over the control period at this time, as will be seen from the table. During the second control period, that is, after discontinuing the calcium, the coagulation time again returned to two and one-half hours.

The calcium determinations in the blood, urine, feces and food extended over a period of fourteen days. The patient was given a cathartic and put on a milk diet, 7 ounces (210 c.c.) accurately measured every two hours for eight feeds, or 56 ounces (1,680 c.c.) daily. The child was kept on this diet for two days before the determinations began.

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* From the Department of Pediatrics, University of Michigan Medical School.

H. Lyman's[1] turbidity method was employed for the calcium determinations. In the case of the feces, blood, and milk we substituted and adapted to our use an oxidation method in place of the incineration method usually used. This method was originated by Professor Willard of the department of chemistry for the estimation of the mineral content of coal and other organic material, the details of which are not yet published.

The first five days' determinations constitute the first control period, the following days the calcium feeding period, during which the patient received calcium lactate, as indicated in the table. Thirteen per cent. of calcium lactate is calcium. Twenty-six gm. of calcium lactate was to have been given dissolved

CALCIUM DETERMINATIONS IN THE FOOD, URINE, FECES AND BLOOD

Day	Period	Food (Milk)		Urine			Feces		Calcium in 1,000 C.c. Blood, Gm.	Coagulation Time, H. M.
		Per Cent. Calcium	Total Calcium, Gm.	C.c.	Per Cent. Calcium	Total Calcium, Gm.	Weight, Gm.	Total Calcium, Gm.		
1	Control	0.343	5.0421	297	...	0.10048	32.01	0.5479	.....	....
2	.....	0.322	5.2245	1,030	...	0.482	.....	.....	0.6482	2:35
3	.....	0.344	5.3804	320	...	0.2322	.....	.....	0.6828	2:32
4	.....	0.329	5.3742	1,044	...	0.7471	128.6972	3.4045	0.66	2:48
5	.....	0.345	5.3944	832	8†	0.5578	.....	.....	0.6866	2:35
6	Calcium *	0.349	5.5522	545	...	0.3777	63.334	1.85644	0.6274	1:50
7	*	0.347	5.4256	545	...	0.3277	110.9778	2.4282	0.658	3:30
8	.....	.....	.....	.....	...	.....	.....	.....	.....	....
9	0.65 gm.	0.351	5.9085	744	...	0.5016	277.02	6.7102	0.665	3:00
10	0.91 gm.	0.343	5.4537	855	...	0.5921	.....	.....	0.6844	2:38
11	1.17 gm.	0.345	5.8111	635	...	0.4519	37.338	0.6372	0.7192	4:55
12	1.56 gm.	0.344	5.7926	942	1.5	0.6337	92.141	2.3703	0.7545	4:35
13	Control	0.344	5.7879	772	...	0.5241	260.1684	2.7117	0.6918	2:45
14	.....	0.345	5.8044	797	8	0.5102	99.875	1.814	0.6612	2:15

* The patient vomited the calcium lactate. The calcium was calculated as 13 per cent of the lactate.
† Percentage of total periods.

in distilled water. This was equivalent to 3 gm. of calcium. After the first dose of 7 gm. of calcium lactate the patient complained of considerable epigastric pain, and vomited a small amount. The calcium had to be discontinued. On the seventh day 12 gm. of calcium lactate was to have been given in divided doses of 4 gm. each, but after the first dose the same symptoms recurred. The patient was then given a one-day period of rest from the lactate, during which the milk diet was continued. No determinations were made on this day.

On the ninth day the patient was given 1 gm. of calcium lactate every two hours for five doses, which is equivalent to 0.65 gm. of calcium. On the

1. Lyman, H.: Jour. Biol. Chem., 1915, xxi, 551.

tenth day 7 gm. of calcium lactate were given, 0.91 gm. of calcium. On the eleventh day 9 gm. of calcium lactate were given, 1.17 gm. of calcium; and on the twelfth day were given 12 gm. of calcium lactate, 1.56 gm. of calcium. This was followed by a control period of two days.

The accompanying table records the determinations made. The calcium content of the food (milk) was quite constant, as will be seen from the percentage of calcium in milk given in the table. It should be stated that these estimations make the calcium content of milk slightly higher than the figures usually given, which are from 0.149 to 0.198 per cent. The calcium content of the urine was apparently unchanged by the administration of calcium by the mouth. The blood calcium increased perceptibly but slightly during the calcium feeding period. The data obtained from the feces are of doubtful value, not because of the method of analysis, but because of our inability to obtain daily stools on account of constipation, and because we erred in that we did not mark the stools. We hoped that the preliminary period of milk feeding before the estimations were begun and the long periods of control and of calcium feeding would enable us to obtain averages which would be of more value than one or two day observations. We were particularly interested in the blood calcium and these data, like those of the milk and urine, we believe are trustworthy and of value.

The following conclusions seem to be justified:

1. The calcium content of the blood in this case of hemophilia is the same as that obtained under normal conditions.

2. The calcium content of the blood increased perceptibly during the calcium feeding period.

3. The coagulation time of the blood was lengthened during the calcium feeding period.

4. The calcium content of the food (milk) was slightly greater in our series than in the usually reported analyses.

DISCUSSION

DR. HESS: So far as I know, this is only the second instance in which a study of calcium metabolism has been made in a case of hemophilia. In the cases that I reported some time ago there was one typical case and one atypical. The normal one showed about the same calcium content of the blood as did the case reported by Dr. Laws. In the other case there was what might be termed "hemophilia calcipriva," that is, there was a deficient amount of calcium in the blood, which was increased when calcium was administered by mouth. The coagulation time was also hastened by adding calcium to the blood in vitro. Dr. Laws in his paper did not tell us about the coagulation time of the blood after the sixth day. He did not say whether coagulation was more or less rapid in the following period.

With this type of hemophilia there is a normal calcium content of the blood, yet there is a delayed coagulation time. It might be well to examine, not only the coagulation time, but also the platelets; because in some hemophiliac

families the female members showed abnormal platelets, some of which were very small, and some very large. Observations made since this time tend to confirm this opinion.

DR. COWIE: With regard to Dr. Hess' question, I would say that the coagulation time refers to the coagulation time previous to the administration of calcium and after the administration of calcium. The calcium seemed to lengthen the coagulation time. The platelets were normal in this case, as is usual in cases of hemophilia. We have not gone into a full discussion of the case from the standpoint of coagulation, etc. We were particularly interested in working out the calcium metabolism so far as we could, and in getting a method that would enable us to handle the calcium estimations more easily. We had experienced some difficulty in ashing the blood, and in this process spoiled many of our silica dishes, which were hard to get. In some instances we had to burn as long as twelve hours under a Meeker burner. I set about to find, if possible, some method that would cut out the long incineration, and on inquiry in our department of chemistry, found that Professor Willard had been working on an oxidation method for the estimation of the mineral content of coal, etc. Professor Willard is able to convert coal and other organic matter into a perfectly clear liquid in a comparatively short time. His work is not yet published, but he kindly permitted us to see what we could do with the adaptation of this method to our purpose. We are now able to take 5 c.c. of blood and obtain a perfectly clear fluid in twenty minutes, or, running two samples together, in thirty minutes. By this method the calcium in a 5 c.c. sample of blood is obtained in a perfectly clear solution amounting to from 1.5 to 2 c.c. We have not worked out the final details of the method yet, but expect to do so shortly.

THE CALCIUM CONTENT OF THE BLOOD IN RACHITIS AND TETANY*

JOHN HOWLAND, M.D., AND W. McK. MARRIOTT, M.D.
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Glisson was the first clearly to describe rickets, but he apparently described healed cases, with great deformity of the bones, because he expressed his belief, that the bones were as firm as those of other children. Jean Louis Petit in 1733 called attention to the pliability and fragility of the bones in this disease, but it was not until the observations of Friedleben in the first half of the nineteenth century that it was clearly understood on what this lack of firmness of the bones depended. Friedleben determined the mineral content of the bones in rickets and showed that the salts were very deficient and that it was particularly the salts of calcium that were diminished.

The pathologic studies of Pommer, Schmorl and Schmidt have been especially illuminating in that they have shown that not only the changes in the shaft, and so the flexibility of the bone, depend on the lack of calcium, but that the changes in the epiphyses also depend on an insufficient amount of calcium, and it is the changes in the epiphyses that give to rickets its specific character.

Under normal circumstances the intercellular substance lying between the cartilage cells nearest to the epiphyseal line becomes impregnated with the salts of calcium, and thus firm, unyielding lines of direction are given to the blood vessels sprouting up from the marrow. These blood vessels destroy the cartilage cells by erosion. Now in the case of rickets the calcium is absent, and the intercellular substance offers no resistance to the loops of blood vessels. Thus these vessels grow in all directions and are not directed against the cartilage cells. The cells escape erosion and are able to continue their existence. Because they continue their existence beyond their normal limits the erroneous impression has arisen that there is an overgrowth of cartilage. Furthermore, whatever bone is formed in the vicinity of this epiphyseal line is poorly infiltrated with calcium. All new bone as it is formed goes through the stage called osteoid, which, in the language

* From the Harriet Lane Home and from the Department of Pediatrics, Johns Hopkins University.

of the present day, might be called near-bone because all that it needs to make it bone, so far as anatomic studies can demonstrate, is that it shall be infiltrated with lime.

In normal circumstances the bony trabeculae have the narrowest possible margin of this osteoid, whereas the trabeculae in rickets have a large quantity of this immature bone. It really comes down to the question, then, why calcium is not deposited in this immature bone which is prepared for its reception.

Lehnerdt[1] has discussed this question very ably. We may suppose, in the first place, that insufficient calcium is given in the food. This view has been heartily supported by Zweifel, Aron, Sebauer, Dibbelt and rather half-heartedly by Schabad. There are two chief arguments against this theory that not enough calcium is given in the food. The first is that many children develop rickets when they receive a great excess of calcium, as they ordinarily do when they are fed on cow's milk, and the second argument against it is derived from experiments on animals. Animals deprived of calcium in the diet suffer great changes in their bones. These are pliable and soft and grossly they resemble rickets, but microscopically the condition is not rickets, it is osteoporosis. The bony trabeculae are very few in number, but every one is well impregnated with calcium and the changes at the epiphyses are not those of rickets.

In the second place, we may suppose that enough calcium is given in the food, but that it is not absorbed. It is true that more calcium is found in the stools with rickets, enough so that a very distinct negative balance results, but it is impossible to say whether the calcium has passed through unabsorbed or whether it has been absorbed and excreted. Calcium acts like any other of the heavy metals. It is excreted largely by the intestine, no matter how it is given. Thus the chemical examination of the stools does not assist us in answering this question. But again, the evidence against a failure to absorb lime is chiefly that if it were not absorbed the effect would be the same as if it were not given by mouth; osteoporosis would result and not true rickets.

It has been suggested that calcium is absorbed in sufficient amount, but that it is excreted in consequence of abnormal digestive processes in the gastro-intestinal tract that attract the calcium. This does not seem very likely, for if the calcium were circulating in the blood, a large

1. Lehnerdt: Ergebn. d. inn. Med. u. Kinderh., vol. vi.

amount of it in any event would reach the bones before it reached the intestines. It would be deposited in the bones. It is hard to believe that substances in the intestinal tract could have such an attraction for calcium deposited in the bones as to be able to withdraw it from the bones.

All of these theories proving more or less unsatisfactory, it is now believed, and this belief is shared by the best students of rickets, that the calcium which has been absorbed in sufficient amount cannot, for some reason or other, be utilized, and hence is excreted as a useless substance. It cannot be utilized, either because on account of some peculiarity of its combination in the blood it is not available even for normal bone, a very unlikely hypothesis, or, and this seems most probable, because of some inherent trouble in the cartilage or bone itself, they are unable to make use of what is there in sufficient quantity.

It will thus be seen that the present view is derived entirely from indirect evidence. So far as we are aware there have been no studies of the blood in rickets to show whether the calcium is present in sufficient amount or not. The difficulty has been that the amount of calcium in the quantity of blood that can be obtained from an infant is insignificantly small. We have devised, in the last two years, a method which allows us to determine with a sufficient degree of accuracy (that is, with an error of $\pm$ 5 per cent.) the calcium in 1 or 2 c.c. of serum and with this method we have studied the calcium content of the blood of normal children and of those with rickets. It is, of course, difficult to tell whether a child is suffering from active rickets or not. The rickets might be temporarily in a period of remission, with the retention of calcium and deposition of this in the bones and cartilage. The studies of Schmorl have demonstrated beyond peradventure that such remissions are possible. But if a sufficient number of cases are studied, and particularly if children under a year of age, and during the winter months, are used for the study, there is every reason to believe that a large proportion of those with the clinical evidences of active rickets would actually have active rickets. We have, therefore, studied eleven cases of rickets after determining on a number of normal controls the calcium content of the blood.

We have examined three samples of placental blood and we have examined the blood of six normal infants and three adults. It is quite surprising how closely the results agree. With one exception the calcium content calculated in terms of 100 c.c. of serum, is from 9.8 to

11.3 mg. (Table 1). When we turn to rickets we find that there is in some instances a reduction in the calcium, but the reduction is very slight (Table 2). Never have we found in rickets less than 9 mg. per 100 c.c. of serum and in most instances the amount is over 10 mg. So that we can say definitely at the present time that rickets does not depend on an insufficient quantity of calcium circulating in the blood. It appears more likely that the disturbance is primarily one of the cartilage and bone, which prevents the utilization of the calcium brought to them in sufficient amount.

TABLE 1.—CALCIUM CONTENT OF PLACENTAL, INFANT AND ADULT BLOOD IN MG. CALCIUM PER 100 C.C. OF SERUM

	Mg. per 100 C.c.
Placental blood	10.7
Placental blood	11.0
Placental blood	10.8
Normal infant	11.5
Normal infant	11.0
Normal infant	11.0
Normal infant	10.8
Normal infant	11.0
Normal adult	11.2
Normal adult	11.3
Normal adult	9.8
Normal adult	9.2

TABLE 2.—CALCIUM CONTENT OF BLOOD IN CASES OF RICKETS, IN MG. CALCIUM PER 100 C.C. SERUM

Patient	Mg. per 100 C.c.
B. S.	10.9
J. M.	10.0
M. S.	10.9
L. B.	9.1
A. T.	10.9
R. W.	9.0
L. W.	10.5
F. F.	9.0
H. L.	9.0
G. L.	11.0
E. F.	9.0

The close association of tetany with rickets has long been recognized, but it has also been appreciated that there is some peculiarity that determines the onset of convulsions, laryngospasm and the other evidences of tetany, for these occur, not with the most marked, but with the mild or moderately severe cases of rickets. It has been suggested that the same calcium disturbance would be found with both of these conditions. As we have just seen, the calcium content of the blood

in rickets is little if at all affected. So far as we have been able to determine nothing was done to investigate the metabolism of calcium in tetany until MacCallum and Voegtlein, in their study of parathyroidectomy on the production of tetany in dogs, determined the calcium content of the blood in normal dogs and in those with tetany. They found that when tetany appeared the calcium content of the blood was reduced to about one-half the figures for the normal amount. It required 100 c.c. of blood to make the determinations, and for obvious reasons these determinations were not repeated on dogs, nor have they been attempted on man.

Leaving entirely out of consideration the question whether tetany in infants is dependent on a deficient function of the parathyroid glands or not, it is of the greatest importance to determine if the calcium of the blood regularly is low; not only for a clear understanding of the character of the disease, but also for eminently practical reasons, for it seems not entirely unlikely that some of the most severe symptoms, such as muscular spasms, might depend directly on a low calcium content of the blood, and it has been shown by MacCallum and Voegtlein that the severe spasms of parathyroid tetany may, to a great extent, be controlled by calcium in large doses. While this effect might be only temporary, it might, nevertheless, be life-saving.

So far as we know analyses of the blood of infants with tetany have been attempted only twice. Cattaneo in 1909 reported the findings in seven children, of whom one was normal, one rachitic, two had active tetany and one was convalescent from tetany. The method of analysis is not given. The results are open to question for this reason, but chiefly because the figures that Cattaneo gives for the normal are nearly 100 times what others have found for the normal. He found a great reduction in the rachitic patient, but an astonishing reduction in tetany, to less than one sixtieth the normal. It is obvious that his results do not merit much consideration.

Neurath used the Wright method for the estimation of the relative amount of precipitable calcium present, an indirect and very inexact method. It presupposes that the clotting depends on a perfectly definite amount of calcium. He was unable to demonstrate any constant diminution of calcium in tetany.

We have determined the calcium in the serum of seven patients with active tetany (Table 3). All these have shown a very marked reduction. With two patients, determinations were made on different days,

when the tetany was active, with nearly the same results. This is an admirable check on the analyses. An analysis was made of the serum of two children with no evidences of active tetany, but with characteristic electrical reactions. The calcium of one of these was moderately reduced, that of the other was within normal limits. A very interesting observation was made on one child who, on March 3 had convulsions, laryngospasm and great hyperirritability to the galvanic current. The calcium content of her serum was very low. Three weeks later, when all the evidences of tetany had disappeared, and when she was gaining weight well, the calcium content of her serum was normal. We therefore may say that tetany differs from rickets in that there is a marked reduction in the calcium of the circulating blood.

TABLE 3.—CALCIUM CONTENT OF BLOOD IN CASES OF TETANY, IN MG. CALCIUM PER 100 C.C. SERUM

Patient	Mg. per 100 C.c.	
H. S.	6.3	
T. W.	6.0	
J. P.	5.7	
J. P.	5.0	
M. F.	6.3	
M. F.	6.5	
E. D.	7.3	
M. G.	6.0	
3/8 S. B.	6.0	
4/3 S. B.	10.4	
J. S.	8.5	(not active)
B. D.	10.2	(not active)

TABLE 4.—CALCIUM CONTENT OF BLOOD DURING CONVULSIONS WITHOUT TETANY, IN MG. CALCIUM PER 100 C.C. SERUM

Patient	Mg. per 100 C.c.
D. N.	10.2
B. S.	10.1

This determination may be of much assistance in diagnosis, in excluding tetany. Two children with repeated attacks of convulsions, but with no other evidences of tetany, have been observed and the calcium content of their serum determined. Both of them were well within normal limits (Table 4). It is quite plain that they have not been suffering from tetany. The obscure cause of their repeated convulsions must be sought elsewhere.

Our findings with children have been almost exactly those that we have obtained with dogs that have developed tetany after parathyroidectomy. One animal before operation had 10 mg. per 100 c.c. of serum;

twenty hours after, 8.9; and six days after, when in tetany, less than 6.8. A second at the time of operation had 10.8, and forty-eight hours after, just before the onset of tetany, 7.3 (Table 5). It is apparent that the parathyroids exert a very profound effect on the circulating calcium, and so far as these observations can they point toward a connection between a disturbance in the function of the parathyroids and the symptoms in human tetany. Further than this it is not possible to go at the present time.

TABLE 5.—CALCIUM CONTENT OF BLOOD OF DOGS IN TETANY FOLLOWING PARATHYROIDECTOMY, IN MG. CALCIUM PER 100 C.C. SERUM

	Mg. per 100 C.c.
1.—Before operation	10.8
After forty-eight hours	7.3
2.—Before operation	10.0
After twenty hours	8.9
After six days	6.8

The method for determining calcium that we have used offers an excellent opportunity for investigating the effects of different therapeutic measures on the tetany of infants, and to this we expect to direct our attention in the future.

DISCUSSION

DR. COWIE: I should like to ask whether all the determinations in regard to calcium were made on the serum. Our estimations were made on the whole blood. I believe it has been pointed out that blood corpuscles absorb a certain amount of calcium. It is interesting to compare the observations on the serum with those on the whole blood. With regard to the retention of calcium in tetany, there seem to be two schools, one believing that there is an accumulation of calcium in tetany and the other that the calcium content of the body is unchanged, or possibly only slightly lowered. The figures of Dr. Howland and Dr. Marriott are interesting in that respect. The calcium content of the blood in its normal condition seems to vary a great deal if we accept the recorded analyses. Neuberg found 2.3 to 36 mg. in 100 c.c. of blood, Wolf 6 to 10 mg., Abderhalden 7.2 mg., Wright 32 to 35 mg., and others have reported similar variations. So, on the whole, the knowledge of the calcium content of the blood under normal conditions is very imperfect. A great deal of work will have to be done before any definite statement be made.

DR. SEDGWICK: We have been very much interested in this question. Dr. Veeder has used the term "spasmophilia" for tetany. In regard to the intake of calcium in the food, Dr. Rodda and I found very high results in our work also. We believe that our findings support those of Dr. Laws in regard to the intake of large amounts of calcium. This is of importance in connection with the results that Blühdom has found from the administration of large amounts of calcium. He gave 5 gm. of calcium chlorid a day to patients under 1 year of age. We have been giving calcium chlorid in such doses. Dr.

Laws spoke of the amount of calcium in calcium lactate. In calcium chlorid there is nearly twice as much. Five gm. of calcium chlorid contains twice as much calcium as 5 gm. of calcium lactate. This gives a reason for the lowering of the electric reaction in children under 1 year by the administration of 5 gm. of calcium chlorid per day, and it is interesting as confirming the work of Blühdom. It may also tend to show why it has not been possible to get the same results with these large doses in rickets as in tetany.

We should be thankful for the method devised by Marriott for his calcium study, as we know how much time it takes for this by the old way. Dr. Marriott gave us a description of his method before publishing his paper, and we are working with it. It is important to show the calcium content of the blood in rickets and spasmophilia, and to control the electric reactions with large doses of calcium.

DR. HOLT: I would like to refer to the use by hypodermic injections of magnesium sulphate in tetany. The dosage is important and patients differ much in their susceptibility. It is possible to paralyze the patient in this way. We have been accustomed to give from 8 to 10 grains of Epsom salt to infants 4 or 5 months old, and from 15 to 25 grains to average infants from 8 to 10 months old. It should be remembered that the anhydrous salt sometimes put up by the druggist is twice as strong as Epsom salt. The effects of magnesium sulphate given subcutaneously can usually be obtained in twenty minutes, and generally will last nearly twenty-four hours. It is seldom necessary to repeat the dose in less than twelve hours. We have used it in various types of recurring convulsions; and in the most severe type. This use of magnesium sulphate is a therapeutic measure that is worth further study.

DR. MARRIOTT: With regard to Dr. Cowie's question as to the relative amounts of calcium in the serum and in the whole blood, it has been found that the serum contains about twice as much as the whole blood, volume for volume, because the corpuscles are calcium free. We have thought it better to determine the calcium in the serum, rather than the whole blood, because the corpuscles represent essentially so much inert material, which would vary with the blood count. The method that Dr. Howland and I have devised is applicable for 1 or 2 c.c. of serum. It is true that the blood clot contains a small and relatively constant amount of adsorbed calcium; but it has been shown that the fibrin is not actually a calcium compound, and that the calcium content of serum is practically constant with normal persons.

EARLY MORNING TOXIC VOMITING IN CHILDREN

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The purpose of this communication is to direct attention briefly to the vomiting of children which not infrequently occurs in the early morning, either before or soon after the first feeding. This vomiting is often of toxic origin, as indicated by the fact that the vomitus after the long night period contains no food residue, if before the first morning feeding, and if after this feeding, only food from this meal. In this respect it is sharply distinguished from the vomiting of undigested and fermenting food in cases in which failure of gastric digestion, from whatever cause, is immediately responsible for the emesis. This latter type of vomiting is more prone to occur later in the day, after the stomach has been taxed by one or more feedings.

That some vomiting is toxic in origin has become more and more apparent with our increased familiarity with the so-called cyclic or recurrent vomiting; yet the cases to which I refer have neither the characteristic histories nor the clinical symptoms and course of the recurrent type.

One typical instance will serve as well as many to represent this class.

In July, 1915, a boy, 3 years old, was feverish during the night. Early next morning, after awakening, he vomited fluid free from food residue. By the time of my visit, about 10 a. m., his bowels had acted from a laxative given the evening before, and the stool had a markedly foul odor and contained some mucus. Free purgation with fluid citrate of magnesia and the administration of salol were followed by defervescence and the disappearance of odor.

Again, in January, 1916, the same boy, having had two recent nasal colds, vomited in the early morning, and had a temperature of about 102. Careful physical examination having revealed nothing of moment, and despite the fact that the bowels had moved normally the previous day, the tentative diagnosis was made of disturbance of the intestinal tract, with the reservation that we might be dealing with the initial symptoms of an infectious cold still prevalent in the household. Calomel was given in divided doses, followed by the citrate of magnesia, which produced several very foul stools with considerable mucus. The fever then fell, and the stools became normal under the administration of salol and 4 minim doses of castor oil.

Similar cases could be multiplied from my own experience, and doubtless from that of any pediatric practice. I have therefore come

to look on early morning vomiting as pointing to the probability of a toxic condition arising in the intestinal tract, in fact, as a sign of value when in doubt as to the condition or the cause of the temperature.

What, then, of the processes which lead to such vomiting, and why should it occur so frequently in the early morning, although it is possible that vomiting at other times of the day may have a similar origin?

When the chemistry of the intestinal tract goes wrong, either slowly and cumulatively, as doubtless usually obtains in recurrent vomiting, or more abruptly with the fermentative or putrefactive processes set up by the aid of bacterial agencies, absorption of some of the products into the circulation is certain. Of the degree of the natural power of the organism to cope with these, either by metabolic or excretory means, we know but little.

Fermentative processes, owing to the irritation caused, are more prone than putrefactive processes to set up a conservative diarrhea in an effort at elimination. With free drainage of the intestinal tract, there is, without doubt, excretion through the mucosa of the intestine which serves to some extent to offset the absorption. But with actual or with relative constipation, and consequently lowered elimination, the positive balance of absorption gains the upper hand. The effects of milder degrees are familiar in the dullness, depression of spirits, headache, lack of appetite, coated tongue, and even some feeling of nausea, in both adults and children. If not too habitual, this syndrome is promptly relieved by free catharsis, which not only prevents further absorption, but opens the channels for active excretory elimination.

The toxemia of recurrent vomiting is probably of gradual and cumulative evolution, coming to a head with the development of marked or relative constipation, or precipitated by some unusual factor, such as fatigue, nervous strain, the onset of one of the infectious diseases, or the taking of an anesthetic. Here elimination is slow and vomiting prolonged. Fever is not a constant symptom.

With a more active and fulminating toxic absorption, such as we may assume occurs with an acute putrefactive process in the intestine, fever is a usual accompaniment, often rising sharply, and if a conservative diarrhea be not quickly established, the gastric mucosa participates in the effort at elimination.

It has been my observation that when a child vomits during the night the vomitus almost invariably contains large quantities of partially digested food, while the early morning vomiting, to which I call

attention, consists only of fluid and mucus, provided the first feeding has not been given. It seems hardly probable that gastric stasis, which so often accompanies acute indigestion or the onset of febrile conditions, could be overcome in the final hours of the night, and the stomach be completely emptied of all vestiges of food before the early morning vomiting occurred.

It is much more plausible to assume that in the early morning type the disturbance of digestion has been primarily intestinal, not gastric; that there is an attempted elimination of absorbed toxic principles by the gastric mucosa; and that these accumulate in the stomach during the hours of sleep when all reflex sensations are more or less deadened by slumber, only to assert their presence on awakening, in nausea and vomiting.

Reaccumulation in the stomach of sufficient quantities to cause a recurrence of such vomiting is comparatively rare during the waking hours. At all events, after the stomach has been emptied by one or two acts of emesis at short intervals, the vomiting has not the persistent character of the true recurrent type. This may readily be due to the difference in the nature of the toxic products in the two conditions, their quantity in the circulation, or their rate of excretion.

If vomiting does not occur before food is taken, it may occur when the first food is given, especially if that feeding is milk. So common is it for children to vomit in the morning, if they vomit at all during the course of minor illnesses, and not toward night, as might readily be expected if due to overtaxing of the stomach, and so frequently will milk, if given at the first feeding, be ejected in large masses, that it has come to be my habit, when in the presence of fever I suspect toxemia, to order for the first morning feeding broth or broth and barley gruel. By thus avoiding the formation of acid coagula, I feel that I have often averted the tendency. Dilution of the stomach contents or the demulcent action of the barley when added may play some part in this result.

A further characteristic of both toxic types of vomiting, as distinguished from that of acute gastric indigestion, is the quicker recovery of the digestive functions of the stomach. In the toxic types the stomach functions are only slightly impaired, and as soon as elimination has been accomplished by free catharsis, and vomiting has ceased, simple food will be received and digested. Appetite, which is the best single indication of digestive capacity, also returns more promptly.

The extreme caution so often displayed in resuming feeding after an attack of recurrent vomiting, and the consequent unfortunate condition of undernutrition so often observed in those whose attacks recur at comparatively short intervals, are both entirely unnecessary. These children should be fed simply, as soon as vomiting ceases; and when appetite returns, diet of a simple character should be abundant. The sole obstacle to such prompt feeding in the acute toxic type is the state of the intestinal digestion, which, differing from the recurrent type, has been acutely disturbed. But with proper elimination and suitable remedies the resumption of ample though simple diet may often be prompt and certainly need not be long delayed, save in case diarrhea or a colitis invites caution during the summer months.

I am not aware that the occurrence of vomiting in the early morning has received any special attention, and present my observations with a view to inviting discussion.

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DISCUSSION

DR. SHERMAN: I should like to ask whether Dr. Southworth had a gastric analysis made of the material thrown up in the early morning. I appreciate the fact that the material which comes up through the act of vomiting may not give an accurate gastric analysis, but it might afford an indication as to the secretion, whether there was hyperchlorhydria or not, and possibly also as to the amount of what you might call the neurotic element or character that there might be in the child. Whether it is true that a hyperchlorhydria or a large amount of the acid secretions will give us a larger clot of milk, such as Dr. Southworth speaks of, or not, I do not know; but if such is the case, the mere sign or symptom of one large clot would indicate that there might be a hyperchlorhydria or excess of the hydrochloric acid combinations.

DR. TALBOT: I should like to know whether Dr. Southworth has tested the urine of these children for acetone in the early morning. I have invariably found acetone; and on giving some food containing sugar, such as orange juice, the vomiting has stopped in a day or so.

DR. ABT: I should be inclined to be skeptical in regard to the gastro-intestinal origin of the vomiting. We know that vomiting arises from a great many conditions outside the gastro-intestinal canal. A child often vomits because he has a nasopharyngitis. Many children vomit in the early morning because of acute nasopharyngitis. In several cases that Dr. Southworth referred to the gastro-intestinal symptoms did not seem sufficient to explain the fever and vomiting; and I should be inclined to think of a parenteral infection as the cause. It is possible that catarrhal inflammation and the accumulation of mucus in the nasopharynx might produce it.

DR. SOUTHWORTH: I have not made such examinations of the vomited matter. I think it probable, however, that some of these children may have had some hyperchlorhydria.

Dr. Talbot asked about tests of the urine for acetone. In a good many children who have various gastro-intestinal disturbances there is unquestion-

ably an odor of acetone to the breath; the urine was not tested for acetone and diacetic acid in the patient described.

Had Dr. Abt seen the case which I related in the paper, he would have had no doubt that the intestinal condition was the cause of the temperature, as indicated by the foul odor of the movements and the mucus. The symptoms all subsided when the gastro-intestinal tract was cleared out. That children cough a great deal from the presence of mucus in the nasopharynx in the early morning is a fact with which we are all familiar; but the patients to whom I refer have not had a cough with any mucus in the nasopharynx that I could recognize or that could have been the cause of the early morning vomiting.

A STUDY OF THE ETIOLOGY OF CHOREA*

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This study was undertaken primarily to determine, if possible, the parts which syphilis and bacterial infection play in the etiology of chorea. Several other subjects, such as the relative frequency of endocarditis and rheumatism in association with chorea and the frequency with which possible foci of infection, such as diseased tonsils and carious teeth, are present in chorea, have also been incidentally investigated. The spinal fluid has also been studied in a number of instances. Twenty-six children, eleven boys and fifteen girls, were studied, their ages varying between 3 and 11 years. One of the children died of chorea and several had a very severe type of the disease, but the course was mild or moderate in the remainder.

THE RÔLE OF SYPHILIS IN THE ETIOLOGY OF CHOREA

According to Flatau,[1] Kowalewsly was the first to call attention to the possible etiologic relation of syphilis to chorea. It was Milian,[2] however, who started the discussion of this question. He presented two girls with chorea, showing evidences of syphilis and having positive Wassermann reaction, before the Medical Society of the Hospital of Paris in 1912. Under syphilitic treatment one of these recovered promptly and the other improved. He argued from these cases that syphilis might be the cause of chorea. A few months later he[3]

* From the Medical and Bacteriologic Services of the Boston Children's Hospital.

1. Flatau: Arch. f. Psychiat., 1894, xxvi, 552.
2. Milian: Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiii, 955.
3. Milian: Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiv, 628.

reported the results of the Wassermann test in thirteen cases of chorea. It was strongly positive in five, partially positive in three, a total of 61.53 per cent., and negative in five. He also studied these cases and two others as to evidences pointing to hereditary syphilis and stigmata of syphilis. He came to the conclusion that the evidence in favor of syphilis was certain in eleven, or 73.33 per cent., probable in two, or 13.33 per cent., and doubtful in two, or 13.33 per cent. The data on which he based his conclusions do not in many instances, however, justify these conclusions to the unprejudiced observer. His paper aroused much discussion, most of which was unfavorable. Comby argued that the presence of a positive tuberculin test would be as good evidence in favor of the tubercular origin of chorea as a positive Wassermann test of the syphilitic origin. He also argued that the fact that both chorea and syphilis are helped by arsenic shows nothing as to the syphilitic origin of chorea. Guillian said that the pathologic anatomy of chorea is not that of syphilis and that syphilis of the nervous system does not act like chorea.

Babonneix[4] then looked over the histories of the last 145 cases of chorea in Hutinel's service and found reasons to justify the thought of congenital syphilis in only thirty-six, or 25 per cent. He remarks that these cases show little as to the etiologic relation of syphilis to chorea and calls attention to the fact that there was sufficient in the histories or physical examinations of the cases of pneumonia to justify a suspicion of syphilis in 18 per cent.

Grabois[5] also tabulated Hutinel's cases, including those of the year following the study of Babonneix, and found thirty-four of 136 cases, or 25 per cent., in which syphilis might be thought of. Certain evidence of syphilitic inheritance was present in but three, or 2.2 per cent., while there was presumptive evidence in twenty-eight, or 20.5 per cent. The Wassermann test was positive in but one of the four cases in which it was tried. Moreover, rheumatism was present in 23.5 per cent. and heart disease in 32.3 per cent. of the cases of chorea in which syphilis might be suspected.

Milian[6] continued his investigations and in 1914 was apparently of the opinion that all cases of chorea are syphilitic in origin. He argued,

4. Babonneix: Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiv, 671.

5. Grabois: Thèse de Paris, 1913. No. 298.

6. Milian: Bull. et mém. Soc. méd. d. hôp. de Paris, 1914, Series 3, xxxvii, 368.

in connection with a case reported by Grenet and Sédillot[7] that a negative Wassermann reaction does not exclude syphilis. A striking thing in all of Milian's work is the lack of Wassermann tests, which were very seldom made.

Comby,[8] as the result of Milian's statistics and opinions, studied thirty-three cases of chorea in girls between 5 and 15 years of age, whom he treated and cured in 1913, 1914 and early 1915. Stigmata of syphilis were present in four and the mothers of seven others had had frequent miscarriages. The Wassermann test on the blood was positive in six, feeble or doubtful in four and negative in twenty-three. The cutaneous tuberculin test was positive in twenty and negative in eleven. He concludes that there is more reason for believing that latent tuberculosis is the cause of chorea than there is for attributing it to syphilis, and states that all that the positive Wassermann tests and the presence of a history suggestive of syphilis or of stigmata of the disease show is that a certain proportion of children with chorea also have syphilis. He does not deny that syphilitic infection may play a part in the production of chorea and believes that the encephalitis of chorea may be due to a variety of causes, among which may be syphilis.

Comby's[9] results having been criticized on the ground that the Wassermann test is sometimes positive in the cerebrospinal fluid when it is negative in the blood; he tested both the cerebrospinal fluid and the blood in seven cases. The Wassermann test was negative in the cerebrospinal fluid in all, while it was positive in the blood in one. It is worthy of note in this connection that Marie and Chatelin* got negative tests in the cerebrospinal fluid in eight and Merklen[10] in one case of chorea.

Koplik[11] made Wassermann tests on the blood in ten cases of chorea and got negative results in eight. The test was unsatisfactory, but not positive, in the others. There was nothing to suggest syphilis in the histories or physical examinations of any of them.

Salvarsan and Neosalvarsan Treatment.—Salvarsan was first used

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* Reference given in Footnote 15.

7. Grenet and Sédillot: Bull. et mém. Soc. méd. d. hôp. de Paris, 1913, Series 3, xxxv, 73.

8. Comby: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, Series 3, xxxix, 238.

9. Comby: Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, Series 3, xxxix, 666.

10. Merklen: Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiv, 628.

11. Koplik: Arch. Pediat., 1915, xxxii, 561.

in the treatment of chorea because of the supposed favorable action of arsenic in this disease, on the basis that, this being the most powerful preparation of arsenic, it should give better results than the other forms of the drug. It was not long, however, before it was used because of the belief of some that chorea is a manifestation of syphilis. Much has been written about the use of salvarsan in this connection on a very slight basis of facts.

Salinger,[12] writing in June, 1912, was able to collect but ten cases treated with salvarsan, those of Bokay, Hainess, Mayerhofer, Dufour and Low, Hahn and his own. Szametz[13] used it in one case, presumably not syphilitic, with good results, while Flatau[14] used it ineffectually in a chronic case, unquestionably syphilitic, as the patient was relieved by mercury.

Marie and Chatelin[15] treated twenty-five patients for chorea with intravenous injections of salvarsan, obtaining favorable results. In eight cases, in which the Wassermann test was tried with the cerebrospinal fluid, negative results were shown. They do not believe that the reason salvarsan does good in chorea is because chorea is syphilitic in origin, but because of the parasiticidal action of the arsenic.

Koplik[11] treated nine patients with neosalvarsan, getting no effect in seven; one developed nephritis, and another had a relapse.

A number of authors have claimed favorable results also from the use of salvarsan by the rectum. This method of treatment is hardly worthy of consideration in comparison with the intravenous method. If salvarsan and neosalvarsan are to be given at all, they should be given intravenously.

It seems clear, therefore, from a study of the literature, that there is very little evidence in favor of the syphilitic origin of chorea and much against it.

Original Investigations.—There was nothing whatever in the history of twenty-one, or 81 per cent., of our twenty-six patients to suggest syphilis. In the others there was a history of miscarriages, two in six pregnancies, one in eleven, one in four, four in five, and five in eleven pregnancies. No one of the patients was born prematurely. The blood of three of the five children in whose families there was a his-

12. Salinger: München. med. Wchnschr., 1912, lviii, 25.
13. Szametz: München. med. Wchnschr., 1912, lix, 2333.
14. Flatau: München. med. Wchnschr., 1912, lix, 2102.
15. Marie and Chatelin: Bull. de l'Acad. de méd., Paris, 1912, Series 3, lxviii, 507.

tory of miscarriages gave a negative Wassermann test, the spinal fluid not being tested in these cases. The blood of one gave a positive Wassermann test; the spinal fluid was not tested in this instance. The blood of the other gave a doubtful reaction on three occasions, while the spinal fluid was negative at one examination. These two children were the only ones that gave either a positive or a questionable Wassermann test in the whole series.

None of the twenty-six children showed any stigmata of syphilis. The Wassermann test was done at the Wassermann laboratory of the Massachusetts State Board of Health on the blood of twenty-five of the twenty-six patients. It was negative in twenty-three, or 92 per cent. It was positive in one, and doubtful in another on three occasions. The Wassermann test was tried on the cerebrospinal fluid, obtained by lumbar puncture, on eight patients. It was negative in all.

Granting that a negative Wassermann test does not absolutely exclude syphilis, it is, nevertheless, very strong evidence against it, so strong that it practically excludes syphilis as the cause of the chorea in twenty-three of these patients. The case against syphilis as the cause of the chorea in these twenty-three children is further strengthened by the facts that none of them presented any of the stigmata of syphilis and in only three of them was there anything in the family history even remotely suggesting syphilis. The presence of a positive Wassermann reaction in one instance and a doubtful one in another does not prove that syphilis was the cause of the chorea in these children, because that proportion of positive and doubtful reactions is no higher than the average for the hospital class of children in Boston and vicinity, and probably not so high. Moreover, the test was negative in the spinal fluid of the child in whom the test was doubtful in the blood, when it would naturally be expected to be more marked in the spinal fluid than in the blood, if syphilis was the cause of the chorea. The spinal fluid was unfortunately not examined in the other case. Furthermore, as Comby has said, a positive Wassermann test in a child with chorea does not prove that the chorea is due to syphilis any more than a positive tuberculin test proves that it is due to tuberculosis. As a matter of fact, twenty-one, or 84 per cent., of the twenty-five children in this series in which the skin tuberculin test was done showed a positive reaction. It would be absurd to assume that tuberculosis was the cause of the chorea in these twenty-one children. A study of these cases justifies the conclusion, therefore, that syphilis seldom, if ever, plays an active part in the etiology of chorea.

THE RÔLE OF BACTERIA IN THE ETIOLOGY OF CHOREA

The close clinical relationship between acute articular rheumatism, endocarditis and chorea, taken in connection with the present conception that acute articular rheumatism and acute endocarditis are bacterial in origin, has suggested that chorea is also bacterial in origin and perhaps caused by the same or a similar organism. Further evidence pointing in the same direction is the frequency with which local foci of infection, notably in the tonsils or in and about the teeth, are found in all of these conditions. For these reasons an increasing number of investigations directed toward the discovery of such an organism or group of organisms have been undertaken during recent years.

Our patients confirm the general belief as to the frequency of the association of chorea with rheumatism and endocarditis, seven of them, or 37 per cent., having had rheumatism in the past or with the chorea. Six of them had acute endocarditis and six chronic valvular lesions, a total of twelve, or 46 per cent. They show also the frequency with which local foci of infection are found in the mouth and throat in chorea. The tonsils were normal in but eleven cases, while they were diseased in eleven, or 42 per cent., and had been removed on account of disease in four others. The teeth were normal in but seven and were carious in nineteen, or 73 per cent. Pyorrhea was present in two of these children and definite pus pockets were found in three others when the teeth were extracted.

A number of investigators have found bacteria in the central nervous system in fatal cases of chorea. Among them may be mentioned Westphall, Wassermann and Malkoff,[16] who isolated a diplococcus from the cerebrospinal fluid and with it consistently produced polyarthritis in rabbits. Poynton and Payne[17] also isolated and cultivated a diplococcus from the cerebrospinal fluid in four cases of fatal rheumatism, in three of which there was chorea at the time of death. They produced twitching movements, arthritis, endocarditis and pericarditis by the intravenous injection of this organism into rabbits. They also demonstrated the presence of this same diplococcus three times in the cerebral pia mater and once in the brain in cases of chorea. They also found them in the brain and pia mater of a rabbit that had shown twitching of the muscles.

16. Westphall, Wassermann and Malkoff: Berl. klin. Wchnschr., 1899, xxxvi, 638.

17. Poynton and Payne: Lancet, London, 1905, ii, 1760.

Bacteriology of the Blood in Chorea.—Other investigators have found micro-organisms in the blood during life. Camisa[18] gives seventeen references to authors who have found microorganisms in the blood of patients with chorea. They were usually found in only one or, at most, three cases. The organisms found were very different—bacilli, staphylococci, diplococci, streptococci. He studied the blood taken from the veins in nine patients varying in age from 6 to 16 years. It is to be noted that they all showed evidences of cardiac lesions. He found a diplostreptococcus, forming short chains, in six cases. The morphologic and cultural characteristics of the organism were the same in all cases. The blood serum of patients with chorea at the height of the disease agglutinated this organism to a moderate degree, more than it did the ordinary pus streptococci. The agglutinating power of the blood diminished with improvement of the symptoms. This agglutinating power was not specific, however, as the organism was agglutinated more strongly by the serum of a typhoid patient. Animal experiments were negative. He believes that this organism is the cause of chorea, but admits that it is possible that chorea may also be caused by other organisms.

Donath[19] studied seven cases of very severe chorea, two of which were fatal. He found the *Staphylococcus pyogenes-albus* in the blood in four cases and in the brain in one case, and the *Staphylococcus pyogenes-aureus* in the blood in one case and the cerebrospinal fluid in another. Animal experiments were inconclusive. He is inclined to think that the staphylococci found were of pathogenic significance, but does not ascribe any specificity to them.

Collins[20] obtained a pure culture of a diplococcus from the blood of a girl ill with chorea. This organism grew in twos and formed short chains of from four to six pairs. A vaccine was prepared from it, which, in his opinion, had a favorable influence on the course of the disease.

Richards[21] made blood cultures from the veins in two cases of chorea. It is to be noted that one of the patients had chronic endocarditis, acute arthritis and pyorrhea alveolaris, while the other had chronic endocarditis and had had tonsillitis. He found the *Strepto-*

18. Camisa: Centralbl. f. Bakteriol., Orig., 1910-1911, lvii, 99.
19. Donath: Ztschr. f. d. ges. Neurol. u. Psychiat., Orig., 1910-1911, iv, 91.
20. Collins: Brit. Med. Jour., 1913, i, 220.
21. Richards: Jour. Am. Med. Assn., 1914, lxii, 110.

coccus viridans in both. He says that there is "no doubt that this coccus found in the blood is associated with endocarditis, but that it is the etiologic factor sine qua non in chorea is not proved."

La Fétra[22] in the discussion of a paper by Strauss stated that he had found the *Streptococcus viridans* in two cases of chorea at the Bellevue Hospital and that complement deviation tests were positive in two others. He does not state in how many instances he obtained negative results. Bartley, in the same discussion, stated that tests made in three or four cases at the Long Island College Hospital were negative.

Koplik[11] states that he has had the blood diligently cultivated in many cases of chorea, but that he has failed to isolate any organisms.

It is evident that the results thus far obtained from blood cultures in chorea are inconsistent and inconclusive. In almost every case in which organisms have been found there has been some other complicating condition amply sufficient to account for the presence of organisms in the blood. Their presence, therefore, has not proved that they were the cause of the chorea. The absence of organisms in the blood does not prove, however, that chorea is not caused by bacteria, because, although the cause of the disease, they may have been absent from the blood at the time the cultures were made, and the methods of cultivation used may not have been suitable for the growth of the organisms, if present.

Bacteriology of the Cerebrospinal Fluid in Chorea.—There are practically no data as to the bacteriology of the cerebrospinal fluid in chorea during life. Donath[19] found the *Staphylococcus aureus* in one case, while Passini[23] found the cerebrospinal fluid sterile in five cases. Collins[20] has reported a case of chorea as cured by treatment with an autogenous vaccine prepared from a coccus obtained by lumbar puncture.

Original Investigations.—We have made during the past year a bacteriologic study of twenty-six cases of chorea in the acute stage of the disease with a view to determining the presence of an infecting agent in the blood stream and cerebrospinal fluid, the frequency with which it could be obtained, and its cultural characteristics. The cerebrospinal fluid was obtained by lumbar puncture under an anesthetic and with sterile precautions twenty times in nineteen cases. The blood

22. La Fétra: Arch. Pediat., 1915, xxxii, 135.
23. Passini: Wien. klin. Wchnschr., 1914, xxvii, 1363.

was obtained from one of the veins of the arm with sterile precautions, sometimes under an anesthetic and sometimes not, thirty-one times in twenty-six cases.

About 5 c.c. of cerebrospinal fluid and 5 c.c. of blood were secured when it was possible. The blood was immediately put into a series of different kinds of mediums and incubated for two weeks. During this time frequent examinations of the cultures were made and fresh transfers were inoculated. The cerebrospinal fluid was similarly treated. The mediums used consisted of blood dextrose agar, Loeffler's blood serum, neutral and acid milk, serum water dextrose, lactose, and saccharose, dextrose bouillon, and at times hydrocele fluid alone and with agar. Aerobic and anaerobic methods were both used. Blood was also drawn into citrated saline solution and centrifuged. The sediment was planted and smears made for examination. In every instance the cultures, as well as smears from the cerebrospinal fluid, were negative. Blood cultures were negative in twenty-six instances, even after several weeks of incubation and subculturing. In five cases organisms were obtained. In one case a small bacillus, diphtheroid in type, appeared, giving a fine, pinpoint, moist growth on blood serum at the end of a week. This organism grew very slowly on agar and failed to produce any reaction in solutions of serum water containing saccharose, lactose, mannite, raffinose, dextrose, inulin, and maltose. It was gram negative and was not pathogenic for rabbits even when large doses were given intravenously. In this instance the tonsils were large and the teeth were slightly carious. The heart was normal and there were no rheumatic symptoms.

Diplococci were found in the blood smears in one case, but no organisms were cultivated. In this instance the tonsils were submerged and there were several carious teeth, one of which had a pocket of pus about its root. The heart was normal and there were no symptoms of rheumatism.

In two other cases short chains of cocci appeared in litmus milk in the initial culture, but all efforts of subculturing failed. The tonsils were normal in both of these cases, but the teeth were carious. The heart was normal in both and neither showed any evidences of rheumatism.

In another case positive blood serum cultures were obtained after ten days of incubation. In this instance the tonsils and adenoids had been removed, but the teeth were carious. The patient had acute

endocarditis and had had several attacks of rheumatism. The first colonies appearing were flat, colorless and disklike. Smears showed these to be made up of long chains of a fine gram-positive streptococcus. Subcultures were at first obtained with difficulty. This organism produced a slight greenish-yellow zone of hemolysis on blood agar plates, fermented saccharose and dextrose in serum water cultures, did not acidulate or coagulate milk, and failed to act upon lactose, mannite, raffinose, inulin, and maltose. This organism is now readily subcultured and its early characteristics have remained unchanged through ten generations. Intravenous inoculations in two rabbits in doses of from 2 to 3 c.c. of a thick suspension of the organism killed the animals in from twenty-four to forty-eight hours. Necropsies showed a general septicemia, and cultures from the heart's blood and knee joints gave a good growth of streptococci. Four other large rabbits were given a series of intravenous inoculations of from 0.5 to 1 c.c. of a heavy suspension of the organism at an interval of from three to five days. Three were killed at intervals of from ten to thirty days. All the animals lost weight and, with the exception of Rabbit 6, which died after five days, they all showed lameness and difficulty in walking and standing and restlessness on handling of the joints. Some swelling of the knees was also noted.

PROTOCOLS

RABBIT 3.—Large white male, showing considerable loss of weight. Opening of the knee joint showed a smooth, glistening surface. There was a moderate amount of fluid in both joints, sticky and turbid. Smears showed numerous leukocytes and chains of streptococci. A good growth was obtained on culture.

The heart cultures gave streptococci. The organ was filled with postmortem clot, but the valves and endocardium were negative. The brain was not examined.

RABBIT 4.—A medium-sized brown male, showing marked loss of weight, was given four inoculations in three weeks' time, each dose consisting of 1 c.c. of saline suspension. The animal was killed while moribund. For two weeks there had been apparent pain and limitation of motion in both knee and hip joints. The knee joints showed a turbid, sticky fluid containing numerous leukocytes and streptococci. Cultures gave the organism in pure culture.

The heart was negative. Cultures from the heart's blood gave chains of streptococci.

The dural and pial vessels about the brain were much engorged. No thickening or exudation was found. Smears gave streptococci in chains, but cultures were negative. Sections were hardened in 80 per cent. alcohol and stained with hematoxylin, eosin and Giemsa stain. Marked round-cell infiltration of the pia extending slightly into the brain substance was noted. There was some increase of leukocytes. No organisms were found.

RABBIT 5.—A large brown and white female was given a series of intravenous inoculations of a heavy saline suspension of streptococcus over a period of five weeks. Marked crippling of the joints of the fore and the hind legs was noted. The animal was killed while in fairly good condition. The heart valves and endocardium were negative. Smears and cultures from the heart's blood were negative. The pial vessels were slightly distended. Smears and cultures were negative. The knee joints both contained a thick, sticky fluid, the left capsule being distended with it. Smears showed numerous leukocytes and chains of streptococci. Cultures of streptococci were readily obtained. Sections of the brain showed marked round-cell infiltration of the pia over the cortex and extending generally into the convolutions. No organisms were seen.

RABBIT 6.—A large, white male rabbit was given 1.5 c.c. intravenously of a heavy saline suspension of streptococci obtained from the knee joint of Rabbit 5. The animal lived four days and then died. The heart showed some enlargement. The valves were negative macroscopically. Scattered over the endocardium, especially in the wall of the left ventricle, were small white areas about 0.1 to 0.2 cm. in diameter. The largest area, 0.2 cm. in diameter, near the mitral orifice, gave a good growth of streptococci on culture. Cultures from the heart's blood were positive for streptococci.

Examination of the brain showed distention of the pial vessels. Smears and cultures from the cortex showed streptococci in abundance.

A series of agglutination tests was carried out, by using a suspension of the organism, together with blood serum or cerebrospinal fluid from eight patients with active chorea. No positive results were obtained.

COMMENT

It is difficult to draw any positive conclusions from the results of our work as to the part which bacteria play in the etiology of chorea. In view of the fact that the diphtheroid bacillus isolated from the first patient was nonpathogenic for rabbits, it seems very improbable that it played any part in the etiology of the chorea in this instance. It seems probable that the cocci which developed in the initial cultures from the third and fourth patients were the same as those which were cultivated in the fifth. There is, however, absolutely no proof that this is so; it is merely a supposition. The diplococcus found in the blood smears from the second patient was evidently a different organism. The fact that the streptococcus obtained from the fifth patient caused lesions in the endocardium and joints of rabbits makes it very probable that it was the cause of the endocarditis in the child. The fact that it caused lesions in the brain and meninges of rabbits, similar to those found in the brain and meninges of fatal cases of chorea, suggests that it was also the cause of the chorea in the child. Further than this it is not safe to go. It must also be remembered that there was a local focus of infection in all the cases in which cocci were found in the blood, and that the microorganisms might have been derived from this

focus and have had no etiologic connection with the chorea. The absence of organisms in the cerebrospinal fluid in all of the cases in which it was examined is also an argument against the bacterial origin of chorea, because it would seem reasonable to suppose that in a disease in which lesions are located in the nervous system the causative organism would be more constantly present and more abundant in the cerebrospinal fluid than in the blood. The absence of organisms in the cerebrospinal fluid and in the blood of most of the patients in this series may be explained, however, by the fact that the majority of the cases were mild or only moderately severe in type. It is also possible that the failure to detect organisms more often, either in smears or cultures from the blood, may have been due to the fact that they are only temporarily present in the blood stream and tend to locate themselves in the meninges, endocardium or joints. If this is so, the opportunity of securing a positive culture from the blood is small, even if repeated invasions of the blood occur.

The conclusion seems justified, therefore, both from the study of the literature and from our own work, that while there is much which points to a microorganism or a group of organisms as the cause of chorea, the bacterial origin of chorea has not yet been proved.

THE CEREBROSPINAL FLUID IN CHOREA

Most of the studies of the cerebrospinal fluid in chorea have been made by French observers. The fluid was studied and the cells counted in most instances in order to prove or disprove the organic nature of chorea, a discussion of which was going on at the time. Dupré and Camus[24] found a very distinct lymphocytosis in the cerebrospinal fluid obtained by lumbar puncture from a boy of 18 years, ill with a very severe chorea. Babonneix[25] found a lymphocytosis in two of five cases. Sicard[26] is said to have found a distinct lymphocytosis in a severe febrile case, which was still present after six weeks. Thomas and Tinel[27] found a distinct lymphocytosis in a girl of 13, ill three months with chorea. They[28] found a similar condition in two of four other patients examined a few months later. Claude[29] found a lymphocytosis

24. Dupré and Camus: Bull. et mém. Soc. méd. d. hôp. de Paris, 1904, xxi, 361.
25. Babonneix: Traité des maladies de l'enfance d'Hutinel, p. 745.
26. Quoted by several authors, reference not given.
27. Thomas and Tinel: Rev. neurol., 1909, xvii, 638.
28. Thomas and Tinel: Rev. neurol., 1909, xvii, 1060.
29. Claude: Rev. neurol., 1909, xvii, 931.

of six or eight cells to a field in one of two children of 18 years after illness of four months. Gatow-Gatovski[30] did lumbar puncture in seven cases and found a distinct lymphocytosis in one and hypertension in one.

Richardière, Lemaire and Sourdel[31] found a lymphocytosis in twelve of fourteen cases and hypertension in ten. The symptoms were relieved somewhat by lumbar puncture in three cases. The fluid was centrifugalized and the drop at the bottom of the tube examined with an oil immersion lens. The decision as to the presence or absence of a lymphocytosis depended on the number of cells seen per field. This is the method which was apparently used by all the French observers and does not seem at all exact. They conclude that there is almost constantly a lymphocytosis in the cerebrospinal fluid in acute chorea and that it is the most constant of the signs of an organic lesion yet discovered.

Negative results were obtained by many other observers. It is probable, moreover, that a much larger proportion of the positive than of the negative results have been recorded.

Deléarde and Valetti[32] found a lymphocytosis in one of ten cases. There was hypertension in some cases. They think that this is of no diagnostic importance, because hypertension is present in many diseased conditions. Prolonged vomiting followed the punctures in several cases.

Comby[9] found 12 lymphocytes per c.mm. in one of seven cases. There was no excess in the others.

Original Investigations.—Lumbar puncture was done twenty times in nineteen of our cases. The cerebrospinal fluid was perfectly clear in every instance. The pressure was apparently slightly increased in one instance. It was normal in all the others. A fibrin clot was never formed. The number of cells per cubic centimeter was counted in ten cases, and was, respectively, 2, 5, 7, 8, 10, 10, 10, 18, 24 and 25. There was, therefore, a slight increase in the number of cells in three of the ten cases, or 30 per cent. The cells were all mononuclear in every case.

Lumbar puncture had no noticeable effect on the symptoms, either for better or worse, at the time or later, in any instance.

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30. Gatow-Gatovski: Thèse de Paris, 1910, p. 386.
31. Richardière, Lamaire and Sourdel: Ann. de méd. et chir. inf., 1911, xv, 276.
32. Deléarde and Valette: Arch. de méd. d. enfants, 1913, xvi, 481.

CONCLUSIONS

Our investigations show that syphilis plays no direct part in the etiology of chorea. Our results suggest that a microorganism or a group of microorganisms may be the cause of chorea. They seem to show that if chorea is caused by a microorganism, the source of infection is ordinarily in the tonsils or teeth. They tend to confirm the belief that there is an intimate relation between chorea, rheumatism and endocarditis.

DISCUSSION

DR. KOPLIK: I agree with Dr. Morse in his conclusions about syphilis and chorea. I have made a number of blood cultures, and in all the cases, so far, I have had negative results. I was interested in the case in which Dr. Morse had a positive result, and I endorse his conclusion that the child had endocarditis, and that the organism found was the cause of both the endocarditis and the chorea in that particular child. We have a number of cases of endocarditis, old and recent, in which chorea was secondary, and we have had some cases of progressive endocarditis in which we have found also streptococcus; but that does not prove necessarily that the chorea in any of the other cases is of bacterial origin. I suspect, however, that our methods must be improved as to blood cultures, and I suspect, also, that there may be bacterial invasion at first, the bacteria disappearing, and leaving behind them the toxin that causes the symptoms. Therefore, in such cases blood cultures remain negative.

DR. ABT: I went over our hospital records for the past twenty-five years and collected 226 cases of chorea, from which we are going to make a statistical report at another society meeting. There are one or two points that occur to me, however, of which I should like to speak.

It seems to me that chorea expresses a state or condition of the nervous system that manifests itself under a variety of circumstances. Chorea is not due to a single cause. I believe that many different factors contribute to the occurrence of chorea. It was surprising to find how infrequently we obtained a history of rheumatism, syphilis, or any other acute febrile disease or febrile reaction. A large number of patients had chorea without any ascertainable history of previous infectious disease that could be in any way connected with the chorea. That startled us and will probably startle every one who hears it. Nevertheless, that was what was shown by our hospital records. It is not necessarily true that all children who have chorea are suffering from infectious chorea. Possibly a certain proportion of cases occur in neuropathic children who are exhausted or fatigued by physical or mental effort and as a result develop chorea; in such instances chorea may occur independently of any previous infection.

DR. HELMHOLZ: Dr. Rothstein at the Children's Hospital, Chicago, reported his experience with chorea, which he has been studying for some years. He had fifteen positive blood cultures, all streptococcus, and he has been able, by injecting these cultures into dogs, to reproduce in them, in many instances, the characteristic muscular twitchings.

DR. LA FÉTRA: In some studies made at Bellevue we have succeeded in recovering streptococcus viridans from the blood of two of these patients. The technic employed has to be very exact, because when the blood from the

same patients was examined by other workers in the same laboratory, it was found that some obtained the organism and others did not. I am told that the failure of the organisms to develop is usually connected with a slightly acid reaction in the culture medium.

DR. VEEDER: We had the same experience as Dr. Abt, and I feel we must look on chorea simply as a syndrome. In every inflammatory condition of the nervous system we find a definite reaction in the spinal fluid at some stage. We have never been able to get a change in the colloidal gold reaction, which seems to indicate that chorea is not primarily an inflammatory condition of the central nervous system.

DR. JACOBI: I do not doubt that the paper of Dr. Morse will be found to contain values in the line of therapeutics. I take it for granted that we are all inclined to look to therapeutics as the end and purpose of our studies. Therefore, I have nothing to say here of the connection between endocarditis, chorea and rheumatism. I went over that in 1875, more than forty years ago, and am very glad to be reinforced in my opinion by the paper of Dr. Morse.

I wish, however, to direct your attention to a paper that I think will appear in a very short time. It will be read, I hope, before the section on diseases of children of the American Medical Association, by Dr. A. L. Goodman, who is the attending physician of the Jacobi children's division of the German Hospital in New York. He has paid a great deal of attention to curing chorea minor, and you know how difficult that is in a great many cases. He does cure it, however, as a rule, within a very few days. I say that deliberately, because I have seen some of his cases. His treatment is a local and general one. His paper, as I have said, will appear very soon, and I wish to say that his method consists in taking blood in sufficient quantity from the choreic child, say 30 or 40 c.c., taking the serum of that blood, which amounts to a little less than half the quantity, and injecting this serum into that child. This, as I can affirm from having seen it myself, is a remarkable method of treatment. Indeed, it looked so remarkable to me that I did not care to accept it at first, and it may appear in the same light to you. Nevertheless, the paper Dr. Goodman will publish will prove to you that the patients all improve somewhat within twenty-four hours, and still more in forty-eight. They are actually cured within a few days or a week.

I have mentioned this here because I think that it is of the utmost importance, not only on account of the fact that chorea is cured, with all its possible consequences, but also because chorea was not expected to be perfectly cured formerly. You take the blood of the choreic child, take the serum of that blood, which amounts to nearly half the quantity of the blood withdrawn, and inject this serum into that same child from whom the blood was taken. That looks miraculous. It looked so to me in the beginning, but does not any more.

DR. MORSE: In relation to what Dr. Abt and Dr. La Fétra have said, I would state that 37 per cent. of these children had rheumatism in the past or with the chorea, while twelve had acute endocarditis or valvular lesions. The tonsils were normal in eleven, diseased in eleven, and had been removed on account of disease in four others. The teeth had been removed in seven, and were carious in nineteen or 73 per cent. Definite pus pockets were found in three when the teeth were extracted. These cases favor the old view of the connection between endocarditis and rheumatism and local foci of infection.

THE EFFECT OF SUBCUTANEOUS INJECTIONS OF MAGNESIUM SULPHATE IN CHOREA

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The existence of the condition termed chorea has been well known ever since the Middle Ages. For centuries the medical profession has endeavored to treat it satisfactorily, as well as to explain its etiology. The results so far have been disappointing. Sedatives, such as bromids and chloral, the salicylates, rest, hydrotherapy, and hygienic measures, all have a beneficial influence on certain symptoms in chorea. Arsenic, however, in this condition is a greatly overestimated drug; I have yet to see it relieve, even in the slightest degree, the choreic manifestations or shorten the course of the disease. We are still sadly in want of a specific remedy to cope satisfactorily with this annoying, chronic, and occasionally serious malady.

In the absence of positive knowledge as to the causation of chorea, it is justifiable to attempt symptomatic treatment alone, with the view of lessening the severity and frequency of the choreic manifestations and rendering the patient more comfortable. Stimulated by the work of Meltzer in the treatment of tetanus by injections of magnesium sulphate, I applied a similar method in a series of chorea cases, in the hope that a favorable influence would be exerted on the psychomotor system.

Meltzer investigated the effect of various salts on animals and human beings and found that of magnesium sulphate unmistakably inhibitory in character. Various modes of administration were investigated—intravenous, intraspinal, intramuscular, and subcutaneous. In intravenous and intramuscular injections the effect was rapid, but of short duration; in intraspinal injections, rapid and of longer duration; in subcutaneous injections, slow and of still longer duration, with the possibility of a cumulative action. Meltzer claims that in tetanus there is no other remedy capable of relieving the very severe convulsive symptoms so satisfactorily as the injection of magnesium sulphate. To explain the inhibitory phenomena exerted by magnesium sulphate in tetanus, he offers the hypothesis that the magnesium solution contained in the lymphatic circulation enters into the spaces, or, as termed by Sherrington, "synaptic membrane," between the various neurons or

between neurons and muscle, and thus interrupts the passage of afferent impulses. He concludes that magnesium sulphate by subcutaneous injections should be given in every case of tetanus.

Chorea, though entirely dissimilar in etiology, in pathology, and in symptomatology to tetanus, is characterized by irregular, incoordinate muscular movements, which in turn depend on some pathologic condition of the psychomotor system, probably central in origin. Reasoning from analogy, therefore, I regarded it possible that magnesium sulphate might have a similar beneficial effect in chorea, and that a trial in a series of cases would be warranted. Feliziani and Natali have used intraspinal injections of magnesium sulphate in chorea with doubtful results. The latter had seven cases of chorea minor and one case of chronic chorea in which this method of therapy was employed. He claims that three patients were entirely, and four nearly, cured, but that the chronic case was not modified. Even if this method of therapy were but empirical and had not a possible theoretical foundation, no apology would be necessary for employing it in an endeavor to find a remedy for this obscure condition which has for so long baffled medical science. That the results were disappointing in chorea does not in any way speak against the use of magnesium sulphate in tetanus, in which disease excellent results have been obtained. If chorea is a direct sequel of rheumatism, influenza, scarlatina, or other infections, it is possible that no remedy will be of any avail until the respective toxins have been thoroughly eliminated from the system in each case, and the damage done to the nervous system healed by the natural and gradual processes of repair.

METHOD AND TECHNIC OF INJECTION

Five successive patients with chorea from the children's service of Dr. Koplik at Mt. Sinai Hospital were treated by repeated subcutaneous injections of magnesium sulphate. In every case a 25 per cent. sterile solution was used. The dose ranged from 0.01 gm. magnesium sulphate per kilogram of body weight (that is, 0.04 c.c. of the 25 per cent. solution) at the beginning of treatment, with a daily increase to 0.2 gm. magnesium sulphate per kilogram of body weight (that is 0.8 c.c. of the 25 per cent. solution) at the termination of treatment. The actual amounts of solution used daily were from 3 to 30 c.c. The injections were given three times daily for from ten to fifteen days, with the ordinary record syringe, into the back, loins and buttocks of the patients.

EFFECT OF TREATMENT

The table gives in brief the important data regarding the cases under observation. In only one of the five patients treated by this method was there a marked improvement after the series of injections, and in this case the choreic movement gradually diminished, the child became less irritable and general improvement was noted. It is very questionable whether or not the improvement was directly due to the treatment; it is possible that it was purely coincidental and the result of natural processes. In the four other cases there was no improvement, the magnesium sulphate having had apparently no effect whatever on the psychomotor system. In all events the results of the treatment in the small series of cases was not sufficiently promising in my opinion to justify a continuation of the treatment.

DATA OF FIVE PATIENTS TREATED FOR CHOREA BY MAGNESIUM SULPHATE

Name	Age, Yrs.	Duration before Admission, Wk.	Severity	Dose $MgSO_4$ per Kg. Body Weight, Gm.	Period, Days	Number of Injections	Results
A. L.	8	3	Moderate	0.01 to 0.2	11	44	No improvement
I. D.	5	2	Severe	0.01 to 0.055	11	40	Slight improvement
B. K	9	5	Moderate	0.02 to 0.2	13	45	No improvement
E. O	10	6	Severe	0.01 to 0.05	11	37	Considerable improvement
E. W.	10	1	Mild	0.01 to 0.2	11	44	Slight improvement

All the patients were girls.

There are, however, certain decided objections to the use of this method. The quantity of solution used, especially at the termination of treatment, is so large that there is a possibility of an inflammatory reaction, even abscess formation. We did not have any accident of this nature, however, in our cases. Occasionally the patients, especially if very young, are likely to be unduly excited by the treatment itself. Another disadvantage is the possibility of having the needle broken off in the tissues during the administration of the solution, on account of the marked restlessness of the patient. Albuminuria has been reported by several observers after the injection of magnesium sulphate. In our cases albumin was noticed in several instances, but this condition

disappeared after a short interval. This treatment, even if effective, would be best employed in hospitals, inasmuch as three or four injections daily by skilled hands would be required.

CONCLUSIONS

Subcutaneous injections of magnesium sulphate, though employed in only five cases, did not produce sufficient improvement to justify further trial.

I take this opportunity to thank Dr. L. G. Shapiro, formerly house physician of Mt. Sinai Hospital, for his painstaking assistance in this work.

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THE PROGNOSIS AND TREATMENT OF BANTI'S DISEASE IN CHILDREN

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Splenic anemia is essentially a chronic disease, the first stage of which usually lasts for about five years, during which time the symptoms are mild; after this period, for two or three years, they steadily become worse until, finally, the syndrome of Banti's disease, that is, hepatic cirrhosis, ascites, and jaundice, develops, and the case rapidly progresses to a fatal termination. Cases have been reported which persisted for from ten to twenty years, but the juvenile type of this disease tends to run a more acute course than the adult form.

If not treated, or treated only medicinally, splenic anemia is almost invariably fatal. No permanent cure by medicine alone has ever been reported, although in some cases there has been slight temporary improvement. Hull reports a case of splenic anemia in which the blood showed hemoglobin 44 per cent., red blood cells 3,880,000, white blood cells 4,600, and polymorphonuclears 66 per cent.

This patient refused surgical treatment, and was given ascending doses of Fowler's solution and Blaud's pills, 5 grains three times a day. Under this treatment the blood picture improved somewhat, changing to hemoglobin 55 per cent., red blood cells 3,950,000, and white blood cells 4,600.

He was under observation for several months in the outpatient department of Jefferson Hospital. He steadily lost weight and ran an irregular temperature, but no signs of Banti's disease were present during this time.

Warren reports a patient with Banti's disease who, on being admitted to the hospital in serious condition, declined operation. Gastric hemorrhages and vomiting of blood took place continuously until death occurred from exsanguination.

Under surgical treatment the prognosis in splenic anemia is rather more favorable than otherwise, the outlook depending on the duration of the disease at the time the spleen is removed. If done early, splenectomy is attended by slight mortality, and in uncomplicated cases a cure may be expected; but when the disease is complicated by other affec-

tions of chronic infectious nature, the value of the operation is questionable.

In children suffering from splenic anemia splenectomy is even more advantageous than in adults, and complete recovery is the rule, with the rapid disappearance of all symptoms. After removal of the spleen the blood picture in most cases more or less approaches normal, but in a few cases it may vary greatly, so that five years may elapse before the differential count becomes normal.

When Banti's syndrome becomes well established, the prognosis is most unfavorable, even though splenectomy be performed, for the vital organs have become the seat of degenerative changes and the liver is cirrhotic. In some cases of Banti's disease removal of the spleen will arrest the development, but it will not cause retrogression of the hepatic cirrhosis.

Recovery from Banti's disease has been reported in a few instances in which the spleen was removed while the cirrhosis was very slight, but these are exceptional. As a rule the mortality is very high when splenectomy is done at this stage, and the results are unsatisfactory, although isolated cases have been recorded of fairly well established Banti's disease in which marked improvement followed splenectomy. In a series of eighteen cases of splenectomy performed at the Mayo Clinic for splenic anemia of varying intensity, there were two operative deaths; one death from hepatic cirrhosis three years after operation; one death from foreign cause two and one half years after operation, and twelve patients in excellent health for from six months to seven years after operation.

Five of these patients presented Banti's syndrome. One of them died under the operation, and four in whom there was evidences of hepatic cirrhosis were in excellent health for varying periods up to seven years after operation. In all of these cases the hemoglobin was below 75 per cent., and the average white blood cell count was 4,200.

Armstrong reports a series of thirty-two cases of splenectomy for splenic anemia, with twenty-three recoveries and nine deaths. Grutzner reports a case of Banti's disease in a girl 10 years of age, who was operated on early, with the result that on the fifth day after operation the number of red blood cells had doubled and soon reached normal.

Caro's patient, a man, on blood examination showed hemoglobin 35 per cent., red blood cells 1,400,000, and leukocytes 2,600.

One year after the operation he had gained in weight, and was

feeling well in every respect, his blood count being hemoglobin 80 per cent., red blood cells 4,000,000, and white blood cells 14,800.

Zancan reports a patient with Banti's disease cured by splenectomy, and Sturgis records an instance in which the patient made a good recovery, and was in excellent health fourteen months after splenectomy for Banti's disease. Sutherland and Burghard report a case of splenic anemia in a girl 12 years of age, whose blood picture before operation showed hemoglobin 56 per cent., red blood cells 2,420,000, and white blood cells 9,800.

Three days after operation it had changed to hemoglobin 76 per cent., and red blood cells 4,700,000.

In another girl 6 years of age the blood picture before operation showed hemoglobin 30 per cent., red blood cells 1,870,000, white blood cells 2,400, and megalocytes and microcytes.

After operation it had become hemoglobin 52 per cent., red blood cells 4,000,000, and white blood cells 10,800.

In both of these cases there was relief of all symptoms following the operation, and recovery was rapid.

In one case reported by Sutherland the patient was perfectly well four and one half years after the operation, and showed no signs of splenic anemia. In not a few cases of splenic anemia which continued under observation there was no sign of recurrence for five years after operation.

The mortality in splenectomy for Banti's disease can not, however, be based on the results in these isolated cases which have been reported, since it is most likely that many fatal cases in this group were not included. Until the year 1908 the mortality following splenectomy for splenic anemia was 17 per cent.; from 1908 to 1912 forty-seven splenectomies were performed with five deaths, this mortality being a little above 10 per cent. But these figures are based on cases in which the syndrome of Banti's disease, that is, jaundice, ascites, and hepatic cirrhosis, was not present.

Roehling collected a series of seventy cases with a mortality of 8 per cent. But these must certainly have been cases of splenic anemia in the early stages, since in Banti's disease the mortality varies from 50 to 70 per cent. Banti estimates it at 50 per cent., and Rodman and Willard at 56 per cent.

Until the year 1908 the mortality in splenectomy for Banti's disease was 72 per cent. From 1910 until 1914 there were sixteen cases

recorded with nine deaths, a mortality of 56.25 per cent. These figures would appear to be correct if the cases of Banti's disease are carefully selected so that splenic anemia is not included in the series. When the pathologic lesions of true Banti's disease are taken into consideration, any mortality rate lower than this is probably to be attributed to errors in diagnosis or to a failure to classify splenic anemias accurately.

In medical treatment iron in the form of Blaud's pills, 1 to 5 grains three times a day and Fowler's solution may be given for the anemia; but this treatment in no way influences the underlying cause of splenic anemia, hence no permanent cure can be effected by this therapy. Salvarsan may bring about temporary improvement, and Roentgen-ray treatment sometimes gives relief for a short time; but these measures are likewise of no avail in curing the disease.

As a surgical treatment splenectomy was introduced by Eppinger, who believed that in all cases of hemolytic anemia a pathologic and increased destruction of red blood cells took place in the spleen. In splenic anemia there is evidently an infectious or toxic process going on in the spleen, which causes fibrotic enlargement and the formation of a splenic hemolysin. Therefore, in these cases removal of the spleen has ample justification, even though it is still a mooted question whether the favorable results of splenectomy are due to regeneration of corpuscles or to decreased hemolysis.

If an abundance of iron is supplied to the system after removal of the spleen, which is the organ in which iron metabolism takes place, polycythemia will result in many cases, and an increase in red cells is always noted at varying intervals after operation; therefore, in splenic anemia iron is undoubtedly indicated, both theoretically and practically.

It is also believed that the cirrhotic changes which in Banti's disease take place in the liver are due to toxins produced by the spleen; this explains the favorable influence of splenectomy on the liver. Splenectomy is, however, both useless and dangerous in cases in which the hemoglobin is below 30 per cent., and the red blood cells are below 2,000,000. The operation should, as a rule, be attempted only when there is no edema, no parenchymatous nephritis, no serious degenerative change in the liver, and while the patient is still able to go about.

In severe cases blood transfusion, if done shortly before the splenectomy, seems to increase the ability of the child to withstand the shock of the operation.

The operation of choice in Banti's disease is splenectomy by

Talma's operation. Among the various other operations suggested are the sewing of the spleen to the anterior abdominal wall and the cauterization of the spleen.

In 25 per cent. of the cases of splenectomy for Banti's disease, there is afterward pain in the long bones, this being probably due to hyperplasia of the red bone marrow. After splenectomy for either splenic anemia or Banti's disease there is always danger of gastro-intestinal hemorrhages or of secondary infection owing to lowered power of resistance. Hemorrhages from the stomach and intestines are most likely to occur during the first two weeks after operation, and must be treated by complete rest for the upper abdomen, by injections of saline or of blood serum, or by direct transfusion.

CASE REPORT

CASE 1.—Marie L., white girl, 7 years old, was admitted to Jefferson Hospital Aug. 11, 1915, for swelling in the abdomen and attacks of nose bleed. The family history was absolutely negative. Both father and mother were living and well; father had nose bleed when a young man. Marie is the ninth child; five brothers and three sisters are all well, and none of them has a large abdomen.

The personal history showed that the child was born at full term, and the birth was natural. She was breast fed for the first fifteen months, then bottle fed until she was 2 years old, and after that ate ordinary food, as other children.

She had pertussis when less than 4 years of age, chickenpox at 5, German measles at 6. She never had diphtheria, sore throat, scarlet fever, or pain in the joints. She had an attack of jaundice when she was 3 or 4 days old, which lasted a few weeks, then cleared up, and has never returned. The mother says the child's abdomen has been large ever since she was 2 years old. The appetite has always been fair, but peculiar. The bowels at first were regular, with occasional diarrhea.

Five years ago she had a first attack of nose bleed, which lasted a long time. The nose bled every day for two weeks, and she lost a great deal of blood.

The mother dates the child's illness back to the nose bleed five years ago. Nose bleed persisted off and on until the time of entrance, the last bleeding having taken place Jan. 24, 1915. Hemorrhages are always worse in the summer, and have rarely occurred in cold weather until the past winter, when she had three very severe hemorrhages.

In the spring of 1913 the child had measles, and made so slow a recovery that her physician investigated, and then discovered the enlarged spleen. The child had become very anemic, owing to nose bleeds, several of which necessitated packing of the posterior nares, and the blood then dripped through the packing. In the spring of 1914 she had German measles, which again impoverished her so that she convalesced very slowly. On several occasions in 1913 her mother noticed several hemorrhagic spots under the skin of the anterior chest, which looked like bruises. She has had no bleeding from the gums or the vagina. The mother saw these subcutaneous hemorrhages in the spring of 1914, and not since. The spleen has remained of about the same size.

Last year the mother took the child to Dr. P. B. Bland, who said she had

splenic anemia, and rather favored operation. Dr. Beardsley made the same diagnosis.

The bowels have always been very loose, and recently the stools have been of a light yellow color, but have never been really white. Last March she had several loose bowel movements which the mother says were mixed with a great deal of dark clotted blood; and at that time she vomited a great deal of black material which looked like coffee grounds; she had never done so before, nor has she since.

The mother says the child's general condition is better, but admits that the little girl gets more easily tired than usual. She has had several attacks of palpitation. Her ankles have never been swollen, nor has she ever been very short of breath. The appetite is fair. The mother says she has been growing faster than usual in the last few months. She has never complained of headache,

Fig. 1.—M. J., aged 7 years, splenic anemia. Tracing shows border of enlarged spleen.

nor had any eye trouble; has never had a cough or expectoration, and has not lost much weight. The mother says that several times lately the child has complained of being very tired after extremely slight exertion.

Physical examination revealed an anemic-looking, undernourished child. Protuberances in the abdomen show plainly. The pupils were equal and active, the conjunctivae were pale, and there was a suggestion of icteroid tint to the sclerae. The teeth were fair. The mucous membrane of the mouth was generally pale, the tongue clean, with no tremor. There were no palpable glands in the neck. The thyroid could not be felt. The pulsation of vessels at root of neck and of the jugulars was perceptible.

The expansion of the thorax was fair, and there was no apparent dyspnea.

There was some prominence of the superficial veins. The lungs were clear and resonant throughout, except at the lower left axilla, where there was dullness and absence of breath sounds. There was a diffuse visible cardiac impulse in third and fourth left interspaces, most palpable in the third interspace in the nipple line. On auscultation a thrill was felt. The heart sounds were rapid. There was a presystolic murmur at the mitral area, with sharp second sound. The pulmonic second sound was accentuated. The heart showed displacement upward.

The abdomen showed marked proturbances, mainly on the left side. The splenic outline was visible on right. There was a marked prominence of the abdominal superficial veins. Splenic dulness began in the fifth interspace in the midaxillary line. The left border seemed to be on a line with the posterior axillary line, beginning about two finger-breadths above the xyphoid, and curving out to the right until, at the level of the umbilicus, it is approximately three inches from that spot; the spleen fills almost the entire abdomen. The transverse diameter of the spleen at the umbilicus was, roughly, 11½ inches; the vertical diameter was practically 9 inches. There was dulness at Poupart's ligament on either side. The spleen is firm, notch easily felt, the gland not tender, and freely movable. The liver dulness apparently was not increased. There was no evidence of any fluid in the peritoneal cavity.

Externally there were numerous purpuric spots on the lower limbs, especially on the outer surface of the right thigh and the outer aspect of the left lower leg.

LABORATORY REPORTS

On Aug. 12, 1915, the urine was clear, light amber, specific gravity not taken, very slight trace of albumin, no sugar, no crystals, a few urates, urea 1.9 per cent., no red blood corpuscles, a few hyaline casts, and 3 to 5 pus cells.

A complete blood count made Aug. 12, 1915, showed hemoglobin 52 per cent., red blood cells 3,300,000, white blood cells 6,200, color index 0.8, polymorphonuclears 58 per cent., lymphocytes 41 per cent., basophils, 1 per cent. The red blood cells show change in size and shape.

Complete count made Aug. 16, 1915, showed hemoglobin 45 per cent., red blood cells 3,320,000, white blood cells 2,400, color index 0.6 plus, polymorphonuclears 55 per cent., lymphocytes 44 per cent., eosinophils 1 per cent. The red blood cells were pale in the center. There was slight poikilocytosis. The staining seems to be normal.

On Aug. 19, 1915, blood count showed hemoglobin 43 per cent., red blood cells 3,370,000, white blood cells 4,400, color index 0.7 plus, polymorphonuclears 57 per cent., lymphocytes 43 per cent., eosinophils 1 per cent. The red blood cells had a pale center. There was slight poikilocytosis, and there were a few macrocytes

The minimal resistance was 0.42 and the maximal resistance was 0.26. This is the resistance to varying strengths of hypotonic salt solution of red blood cells.

The red blood cells begin to hemolyze in a 0.42 per cent. salt solution, hence the minimal resistance is 0.42. The red blood cells are completely hemolyzed in a 0.26 per cent. salt solution, thus maximal resistance is 0.26. The normal minimal resistance is 0.47, and normal maximal resistance is 0.3.

On Aug. 14, 1915, the Wassermann reaction of blood was negative. The hemoglobin was markedly reduced. The number of red cells was usually not below 3,000,000. There was slight poikilocytosis, and normoblasts were present. There was an actual leukopenia, but a lymphocytosis.

On April 28, 1916, the mother wrote concerning the child as follows:

"Marie keeps about as usual. She has had several of those cutaneous exhi-

bitions of internal hemorrhage, but all were slight. Mumps were prevalent in her school last winter; she took cold, and had nose bleed several times, swelling of the glands, high temperature, and was ill for a few days, but this is the extent of apparent symptoms. Once in a while I think she is nervous, but otherwise she keeps as well as the other little ones. She goes to school pretty regularly, gets 100 in her studies, and enjoys every minute of her work. She eats fairly well and sleeps well. She is very industrious. I fear for her when warm weather comes, as it is at this time of year that she always bleeds profusely from the nose."

The patient weighed on Aug. 21, 1915, 45¼ pounds. In September, 1915, she had diarrhea for three weeks. There was bleeding from the nose occasionally, never profuse, except once in December, 1915, when she was home from school for two weeks. Purpura appears occasionally on the back, legs and arms, but never on the face. The bowels are always inclined to be loose.

In February, 1916, she had swelling of the glands of her neck (mumps?), associated with fever and nose bleed. Her weight at the time of examination, Feb. 29, 1916, was 48 pounds 10 ounces. Six months before she weighed 46 pounds, and one year before she weighed 50 pounds.

Occasionally blood-streaked saliva dribbles from her mouth at night, and this past winter she has noticed a slight oozing of blood from the posterior gums.

The blood report of May 1, 1916, showed hemoglobin 70 per cent., erythrocytes 4,460,000, leukocytes 3,500, color index 0.8, polymorphonuclears 61 per cent., small lymphocytes 31 per cent., large lymphocytes 7 per cent., and eosinophils 1 per cent. The red blood cells stained palely, and showed slight poikilocytosis and no nucleation.

The urine report of the same date, May 1, 1916, on the sample of 100 c.c. submitted showed it to be turbid, of a yellow color and urinous odor, no sediment forming, and with a specific gravity of 1.016. The reaction was acid. There were no albumin, no sugar, no acetone, no diacetic acid and no crystals. The urea was 1.3 per cent., and there were a few amorphous urates. There were a few epithelial cells and a few leukocytes, but no erythrocytes and no renal tube casts.

DISCUSSION

DR. KOPLIK: There are many cases of enlarged spleen with anemias in children, and the great question is, what is Banti's disease? Are all the cases reported as such really Banti's disease? In a discussion at the Mt. Sinai conference last week Dr. Mandelbaum said that of all the spleens that he had examined and removed for Banti's disease, only one conformed to the picture described by Banti. In other words, Banti's syndrome, if it really exists, is exceedingly rare. The question is, therefore, how common is it among children? That point has not yet been determined. Dr. Graham raises the question of splenectomy. Probably it would interest him and the other members of the society to know the fate of a child with about the same condition. Dr. John A. Wyeth refused to perform a splenectomy in this case, because the spleen was very large. This child has since grown to manhood and has married. He is an engineer in the civil service, and is in apparent health and perfectly happy. He has his large spleen and a large liver. There is no ascites yet, but he has developing glands under the clavicle which show progress of the process. If we had taken out the spleen when he was 8 years of age, he might have lived until now, and possibly have been improved; but this case shows what may happen if the spleen is let be in a case of this kind.

FAMILIAL ICTERUS OF NEW-BORN INFANTS

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Pfannenstiel[1] gave the first detailed description of familial icterus of new-born children. He described two fatal cases and collected the scattered reports in the literature. The cause of familial icterus of new-born children is unknown. The disease has nothing in common with Buhl's or Winckel's disease. There is no evidence to prove that familial icterus is due to septic processes. It is not present at birth, but appears during the first days of life. In none of the cases is there a history of birth injury, nor does it seem to be due to toxemia of pregnancy. Most of these children are strong, robust and mature at birth. One might say that the children are in a sense physically defective and very soon become incapacitated to carry on extra-uterine existence. It is possible that the liver failed in the performance of its extra-uterine function.

The disease may occur in successive pregnancies. Occasionally normal children are born, and later children die a few days after birth as the result of a grave and progressive icterus. As a rule, there is no hereditary influence, nothing of a similar nature is discovered in the family of the father or mother. The disease begins usually on the first or second day of life and rapidly increases in severity. Pfannenstiel briefly described the symptoms by referring to the presence of catarrhal conditions of the mucous membrane, sometimes with bloody discharge, though true melena does not occur. The stools are catarrhal in character and are frequent; the urine contains bile pigment; the patient may show meningeal irritation, with characteristic crying and whining. At the onset there may be hyperemia of the skin. If the disease continues, hemorrhages from the various mucous surfaces and into the skin, as well as from the umbilicus, occur; death follows soon from collapse. Atonic convulsions, particularly of the upper extremities, as well as opisthotonos, are frequently observed. Pfannenstiel

1. Pfannenstiel, J.: Ueber den habituelle Ikterus gravis der Neugeborenen, München. med. Wchnschr., 1908, lv, 2169, 2233.

called attention to the fact that the disease bears no relation to syphilis, and in one case in which a necropsy was made and the liver and the spleen were examined histologically, no evidence of syphilis was discovered, and no spirochetes were found.

Knopfelmacher,[2] who reviews the literature in a critical way, is inclined to think that after all some septic process might be invoked to explain this group of cases. For example, in one of Pfannenstiel's reported cases pericarditis, hemorrhages into the serous cavities and swelling of the kidneys led him to think that possibly an infection had taken place. He even thinks that the habitual occurrence of the disease in the same family is not sufficient argument against the consideration of sepsis. He considers that a chronic infection of the vaginal portion of the birth canal of the mother may serve as the origin of infection in the successive cases.

I should be inclined to believe from my own observation that the septic nature of this disease has not been proved.

The familial form of the disease is not a frequent one if we may judge from the reports of clinicians. Thus, H. Rehn[3] of Frankfort, in connection with a clinical report on one case, remarks that it is rare, and he states that in his fifty years' practice he had not met any similar cases until this one.

The disease under consideration, that is, familial icterus of the new-born, has nothing in common with chronic family jaundice, which is characterized by the fact that it may be present at birth, and it may persist throughout life, or that it may first occur during adolescence. In chronic jaundice the patient experiences but little inconvenience and may attain an advanced age. The enlargement of the spleen in chronic jaundice is a constant feature. Familial icterus of the new-born must also be differentiated from congenital obliteration of the bile duct. This obliterating disease is characterized by intense obstructive jaundice.

Isolated cases of habitual familial jaundice are described in the literature. McGibbon[4] records a family of six children, the oldest of

2. Knopfelmacher: Der habituelle Icterus neonatorum gravis, Ergebn. d. inn. Med. u. Kinderh., 1910, v, 205.

3. Rehn, H.: Zur Kasuistik des habituellen familiären Ikterus der Neugeborenen, Jahrb. f. Kinderh., 1912, lxxv, 358.

4. McGibbon, John: Fatal Cases of Jaundice in the New-Born Child, with Notes of a Case in Successive Pregnancies, Edinburgh Obst. Soc., 1912-1913, xxxviii, 285.

whom was normal, the other five having jaundice. The fourth child was prematurely born; the other four children died of severe icterus between the third and seventh day of life.

Cornelius May[5] described a family in which the father and mother were perfectly normal, with no infections and no syphilis. The first child, born at full term and apparently normal, developed icterus in twelve hours and died on the third day. The second child, fairly well developed, born one year later, apparently normal, became icteric in six hours and died in two days. The third child, born three years later, apparently normal, developed intense icterus in twenty-four hours. The mother began to secrete breast milk on the third day, though the baby seemed too weak to nurse. The neck became rigid, the child cried and whined, convulsions occurred, and with increasing coma death followed on the twelfth day after birth. The necropsy showed no tissue changes or bacteriologic findings. The fourth child, born after three years, gives a very similar history. It developed icterus on the second day. The child was given breast milk, but gradually lost in weight, became comatose and died on the sixth day.

Postmortem examinations have shown a peculiar icteric discoloration of the larger nuclei in the basilar portion of the brain and also a yellowish discoloration of the nuclei in the medulla. This has been described as nuclear icterus. In some instances the cells in the anterior gray portion of the spinal cord are stained yellow. Orth observed the same condition in the brain cells of children who suffered from the milder form of icterus neonatorum.

Pfannenstiel considers that the most important anatomic changes which exist in the so-called nuclear icterus (Kern icterus) are swelling of the spleen, hypertrophy of the liver without microscopic alterations in the structure of the organ, and a tendency to transudations into the serous cavities and into the ventricles of the brain. Catarrhal conditions of the mucous membranes in the digestive tract and minute hemorrhages on the serous and mucous surfaces are recorded, though fatty and other degenerative processes of glands and organs are absent.

I have encountered examples of familial icterus of the new-born in two families. The first case occurred in an Italian family. The baby in question was referred to me through the kindness of Dr. DeLee of the Chicago Lying-In Hospital and Dispensary. The history is as follows:

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5. May: Beitrag zur Kenntnis des Ikterus Neonatorum gravis, Arch. f. Kinderh., 1911, lvi, 313.

The mother and the father were 28 years of age. They were both born near Naples, the mother having lived in this country ten years and the father fifteen years, and they had been married nine years. The mother had pneumonia five years before and was very ill at that time. She had never had any surgical operation, and with the exception of the illness mentioned above, she had always been well. She had four brothers and one sister living and well and in none of their families had a similar diseased condition occurred. The mother's mother died the year before of pneumonia. The mother herself had been well during all of the previous pregnancies. The father's mother was living and well; his father died in Italy from some unknown cause. The father, a barber by occupation, said he had never been sick. The mother had borne five children, of whom two were living and three dead. In addition to this there had been two miscarriages, each occurring at three months. These constituted the second and fourth pregnancies. The first and the second babies were born well and remained so up to that time. The third baby seemed strong and robust at birth, but developed jaundice on the second day and on the third day the jaundice had deepened greatly, the baby being more or less comatose, having frequent convulsive attacks and dying on the third day. The fourth baby sickened on the second day, jaundice becoming intense, convulsions ensuing and death occurring on the third day, as in the previous case.

The family came under my observation with the birth of the fifth child. The history of the last baby does not differ materially from those already described. The child sickened on the first day, icterus became very marked, the child vomited occasionally, bowel movements became somewhat frequent, there was no elevation of temperature, convulsions occurred on the second day, and the child became comatose and died on the fourth day.

The second case occurred in a Russian Jewish family. The father had always been well and denied venereal infection. The mother had had the usual diseases of childhood. Six years before, on account of abdominal pain and symptoms referable to the gallbladder, an operation was performed and the gallbladder was removed. Two or three months after this operation her tonsils were removed. The mother was about 32 years of age and the father was three years her senior. She had borne six children. When her first baby was born the mother was about 21 years of age. This child, a boy, is living and is 11 years old. He had scarlet fever when 6 years of age. His urinary examination shows albumin and casts, and he has a chronic nephritis. The second child is living and well. The third pregnancy resulted in a miscarriage. The fourth child was born robust, but became jaundiced on the second day, was seized with convulsions, had frequent stools, the jaundice became more and more intense, and he died on the third day. I was enabled to examine the fifth child. The mother was delivered at Michael Reese Hospital in May, 1914, in the service of Dr. Lester E. Frankenthal. The child was born apparently well and strong. On the first day he developed jaundice, which rapidly became intense; hemorrhages occurred from the nose and throat and under the skin, and convulsions took place at intervals; vomiting and diarrheal stools were observed, and the baby died on the third day. A necropsy was performed, which showed some enlargement of the liver and spleen, though no other pathologic changes of any moment could be noted and bacteriologic examinations showed the tissues to be sterile. The bile passages were of normal size and showed no obstruction.

The sixth baby was born April 22, 1915, in the service of the Chicago Lying-In Hospital and Dispensary. Delivery was rapid and easy, and there

was no asphyxia at birth, the child crying vigorously. The baby became icteric on the second day. The umbilical wound was normal. The child voided bile-stained urine, but had the normal number of stools. The temperature was about 99. The child resented palpation of the abdomen, and it was thought that there was some tenderness over the liver. The baby cried much and the jaundice deepened materially. The child slept most of the time, nursed very poorly, did not take water, and whined weakly. The conjunctivae became icteric and the yellowness of the skin increased markedly. The urine decreased in quantity, the temperature remained at 99, and the baby seemed very somnolent and toxic. There were no petechial spots and no hemorrhages. On the fourth day the temperature was still 99 and the icterus was more marked. The baby refused food, except as it was forced. The liver was enlarged, but the spleen was not palpable. The somnolence increased and the condition seemed grave. On the fifth day the baby had improved slightly, but icterus was still marked. The child took food more readily, and the urine was voided more frequently and in larger quantities. The baby seemed better, and from this time on the jaundice disappeared gradually. The baby nursed more normally and continued to improve. The child is now over a year old and seems unusually bright and happy, having had no illness of any consequence since then.

CONCLUSION

These reports relate the occurrence of a rare disease in new-born children, characterized by progressive icterus occurring in successive pregnancies and of unknown origin. The disease nearly always terminates fatally, though one of my patients recovered after a most serious attack and with the most alarming symptoms.[6]

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6. In addition to the references already given, the following will be found of interest:

Hichens, P. S.: Cases of Familial Jaundice, Proc. Roy. Soc. Med., 1912-1913, vi, Section of the Study of Disease in Children, p. 197.

Busfield: A Series of Cases of Icterus Neonatorum in a Family, Brit. Med. Jour., 1906, i, 20.

Cruse: Beiträge zur Kenntnis des Ikterus Neonatorum, Arch. f. Kinderh., 1880, i, 353.

Lagréze: Ueber habituellen Ikterus gravis der Neugeborenen, Inaug. Diss. Strassburg, 1904.

Duquid, W. R.: A Series of Cases of Icterus Neonatorum, Brit. Med. Jour., 1906, i, 319.

Pfoeltzer, R.: Kernicterus (Schmorl), Ztschr. f. Geburtsh. u. Gynäk., 1914-1915, lxxvi, 685.

Heynemann, T.: Die Endestehung des Ikterus Neonatorum, Ztschr. f. Geburtsh. u. Gynäk., 1914-1915, lxxvi, 788.

Hyppoe, A.: Ikterus Neonatorum und Gallenfarbstoffsekretion beim Foetus und Neugeborenen, München. med. Wchnschr., 1913, lx, 2161.

Esch: Ueber Kernikterus der Neugeborenen, Zentralbl. f. Gynäk., 1908, xxxii, 969.

Maliwa, E.: Beitrag zur Kenntnis des Icterus Neonatorum, Med. Klin., 1913, ix, 297; Deutsch. med. Wchnschr., 1913, p. 154.

DISCUSSION

DR. SHERMAN: The last speaker mentioned the subject of poisoning as the cause of these jaundices; and Dr. Abt, in his paper, mentioned the fact that there was no degeneration of the various organs, that there was no fatty degeneration, nor even of a milder stage. I do not know, but it has occurred to me, and it is one of the subjects that Dr. Snow and I thought that we might work up, to consider whether these cases of jaundice in this and allied conditions might not be due to the poison of chloroform. We all know that this drug has a tendency toward producing hyaline or fatty degeneration, which concentrates in the liver and kidney more than in any other organ, the heart coming next. Why we have sudden death in chloroform anesthesia is hard to explain; but we do know that some of the late deaths after operations, especially when chloroform has been used, are probably due to the degenerative changes produced by the chloroform itself. In investigating or considering cases of this kind, as well as others that result in sudden death within the first few days after birth, I believe that chloroform is a poison that should be particularly considered. Dr. Snow and I, as I said, are thinking of investigating the amount of chloroform these mothers have had during labor. Dr. Abt said that the jaundice seemed to centralize in certain families, and it might be that these women had received a good deal of chloroform. On the other hand, it would not be necessary for them to have had much for the chloroform to have a bad effect on the infants, because sometimes even the first whiff is enough to cause death or bad after-results. I wonder whether Dr. Abt has considered that and knows the amount of chloroform that may have been received by these mothers.

DR. ABT: We had the blood of one or two of these infants examined, and found no fragility or alteration in the red cells. So far as Dr. Sherman's point is concerned, my impression is that these mothers, being primiparae, received very little chloroform; I am certain the first one mentioned received none. In the other mother, my impression is that the delivery took place without chloroform.

Arkwright, J. A.: A Family Series of Fatal and Dangerous Cases of Icterus Neonatorum: Fourteen Cases in One Family with Four Survivors, Edinburgh Med. Jour., 1902, liv, 156.

Ashby and Wright: The Diseases of Children, Northrup, 1900, Ed. 4, pp. 26-28.

Poynton, F. J.: Some Cases of Jaundice in Childhood, Brit. Jour. Dis. Child., 1913, x, 145.

Auden, G. A.: St. Barth. Hosp. Rep., 1905, xli, 139.

Busfield, J.: Brit. Med. Jour., 1906, i, 20.

Beneke, B.: München. med. Wchnschr., 1907, liv, 2023.

Blomfield, J. E.: Brit. Med. Jour., 1901, i, 1142.

Schmorl: Verhandl. d. deutsch. path. Gesellsch., 1913, vi, 109.

Tileston and Griffin: Am. Jour. Med. Sc., 1910, cxxxix, 847.

Hopkins: Am. Jour. Med. Sc., 1913, cxlvi, 726; Proc. Path. Soc. Philadelphia, 1914, xvi, 5.

Richards and Johnson: Jour. Am. Med. Assn., 1913, lxi, 1586.

Jonas: Seltene icterus form beim Neugeboren, Deutsch. med. Wchnschr., 1914, x, 1799.

Ward: Congenital Familial Cholemia Without Splenomegaly, Brit. Jour. Child. Dis., 1914, xi, 214.

OBSERVATIONS ON THE INTRADERMAL AND REPEATED INTRADERMAL INJECTION OF DIPHTHERIA TOXIN WITH REFERENCE TO THE SCHICK TEST*

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The knowledge of the effect of subcutaneous and, inadvertently, intradermal injection of diphtheria toxin on the cutaneous tissue, is as old as the knowledge of diphtheria antitoxin. It was necessarily one of the first observations made during the process of immunization and of testing out the strength of diphtheria antitoxin. A great deal of the knowledge accumulated at that time has a distinct bearing on the interpretation of the phenomena now seen in the cutaneous reaction known as the Schick test.

Soon after the appearance of the reports concerning the clinical value of the intradermal diphtheria toxin test, I became interested in studying the character of the reaction and its behavior under the influence of repeated injections. My interest was held because of the occurrence of happenings analogous to those encountered with repeated injections of horse serum and cowpox vaccine, which had to be explained on entirely different grounds, and also because of the fact, observed so many times in my series of primary injections, that reactions are frequently delayed beyond the usual twenty-four to forty-eight-hour period, to as late as three or four days. Finally, the chief object of my study was to determine if possible, by means of this simple reaction, whether any degree of active immunity could be induced by these infinitesimally small doses of diphtheria toxin.

The enormous change in the biochemic state of the body that is induced by minute amounts of horse serum, egg white, etc., and the well-known peculiar animal racial differences of reaction to injected substances of various kinds seemed to warrant one in devoting some time to this study, even though it had been quite generally admitted

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that the injection of such small doses of toxin as are represented in 0.1 c.c. of the solution used for the Schick test could have no effect in the production of immunity.

Toxin Employed and Method of Injection: The two lots of diphtheria toxin use were kindly furnished by Parke, Davis & Co. of Detroit. The L + dose of Lot 1 is 0.18 c.c., of Lot 2, 0.18 c.c. The minimum lethal dose of Lot 2 was estimated to be 0.0015 c.c. Both lots came from the same original supply. The former lot was not so constantly kept on ice as the latter. Except when otherwise specified, Lot 1 may be understood to have been used. The usual fine, sharp needle method of intradermal injection with an all-glass finely graduated tuberculin syringe was used in making the injections, 0.1 c.c. being carefully injected intracutaneously just beneath the epidermis.

PART I

Of eighty-one persons taken at random, ages varying from 2 days to adult life, in whom careful daily observations and measurements were made, fifty reacted positively and thirty-one negatively. These injections were made during the months of November, December, January, February, March and April, 1914 and 1916.

Of the fifty positively reacting cases, the first evidence of a definite reaction was observed on the first day in twenty-one cases; on the second day in thirteen cases; on the third day in eight cases, and on the fourth day in eight cases.

Of these fifty cases, the height of the reaction (the maximum) was reached on the first day in eight cases; on the second day in ten cases; on the third day in twenty cases; on the fourth day in eleven cases, and on the fifth day in one case.

Of the eight reactions showing themselves first on the fourth day, all faded away very quickly, within forty-eight hours of their appearance. Of the twenty-one first-day reactions, twenty faded away very slowly, many showing distinct discoloration beyond the seventh day; and one, Case 56, showing a faint reaction, faded away quickly; but a note made five days after the injection records a "stain"; it was accordingly regarded as a positive case. Reactions appearing on the second and third day, like those appearing on the first day, also disappeared slowly. These cases will be referred to again under the caption "Successive Injections."

The age incidence of reaction of the eighty-one patients is as follows:

	Positive	Negative	Total	Per Cent.
Under 5 months	4	13	17	23
5 to 12 months	5	1	6	83
1 to 5 years	21	3	24	87
6 to 12 years	13	12	25	52
Adults	7	2	9	77
Total	50	31	81	62

Observations on the Effect of Varying Strengths of Diphtheria Toxin.—In a susceptible person distinct, measurable and typical reactions were obtained with toxin dilutions as high as 1 to 50,000. One-tenth c.c. of this solution represents two millionths of a gram, or two thousandths of a milligram of toxin. By reference to Figures 1, 2, 3, 4, 5 and 6, forearm D. O. W., the progress of the reactions of the six different dilutions may be seen. The amount of toxin contained in 0.1 c.c. of these solutions is as follows:

No.	Dilution	Dose, C.c.	Toxin, Gm.
1	1 to 50,000	0.1	0.000002
2	1 to 40,000	0.1	0.0000025
3	1 to 30,000	0.1	0.0000033
4	1 to 20,000	0.1	0.000005
5	1 to 10,000	0.1	0.00001
6	1 to 5,000	0.1	0.00002

The exact measurements and other daily recorded phenomena of the reactions will be found in Table 1. It will be observed that, as one should expect, increasing concentrations of the solutions, namely, the greater the quantity of the toxin, the more vigorous the action of the toxin on the unprotected cutaneous cells, and vice versa, the less the reaction of the body against the toxin. This distinctive effect of the toxin on the upper skin structures can go on up to the point of producing a large blister, Figures 7, 8 and 9, without producing any appreciable harm to the individual aside from the local discomfort which comes in these cases. A series of thirteen tests was made, 0.1 c.c. toxin (L + dose 0.18 c.c.) of a dilution of 1 to 1,000, that is, 0.1 mg. of toxin being used. The reactions are recorded in Table 2. Large vesicle formations (blisters) were observed in five of these cases, namely, 4, 6, 7, 8 and 13.

So much has been written concerning the character of a typical reaction that I shall refer to but a few points here: (1) the interpreta-

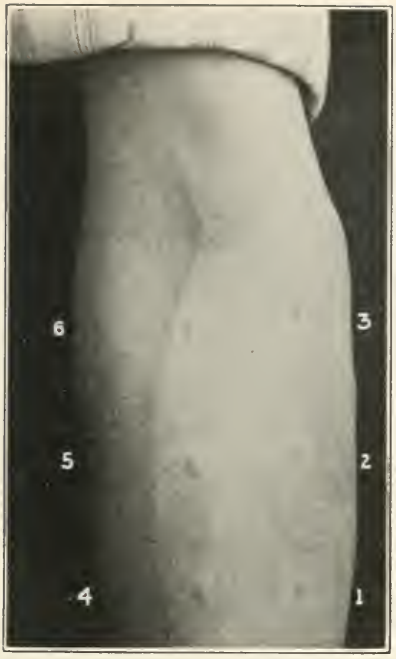

Fig. 1.—Twelve hours after injection. This and the five succeeding illustrations show the progress of the reactions of the six different dilutions: 1, 1 to 50,000 dilution toxin; 2, 1 to 40,000; 3, 1 to 30,000; 4, 1 to 20,000; 5, 1 to 10,000; 6, 1 to 5,000. A reading glass will aid greatly in bringing out the detail of the lesions.

Fig. 2.—Twenty-four hours after injection. Note the slight general swelling. The vein is less visible.

Fig. 3.—Second day. General swelling more marked.

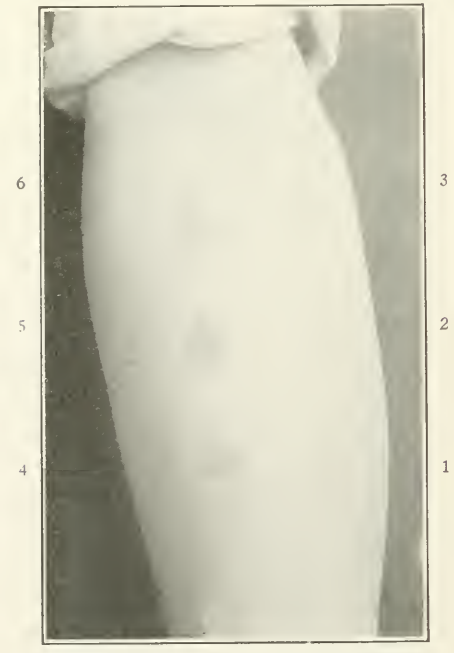

Fig. 4.—Third day. Vein cannot be seen.

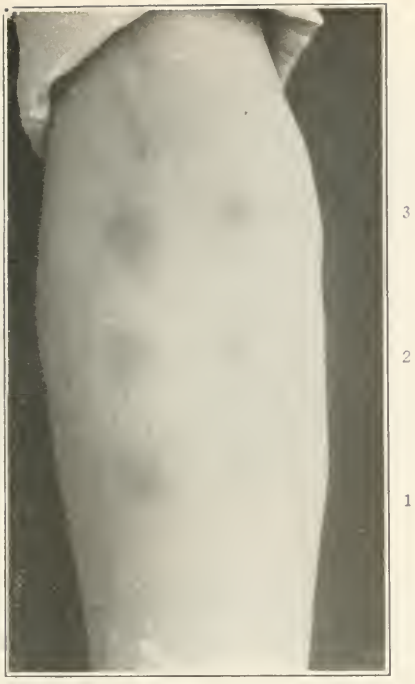

Fig. 5.—Sixth day; 5 and 6 (see numbers as given in Figure 1) show wrinkling.

Fig. 6.—Eighth day; 5 and 6 (see numbers as given in Figure 1) desquamating.

Fig. 7.—Lesion following the intradermal injection of 0.1 c.c. toxin diluted 1 to 1,000.

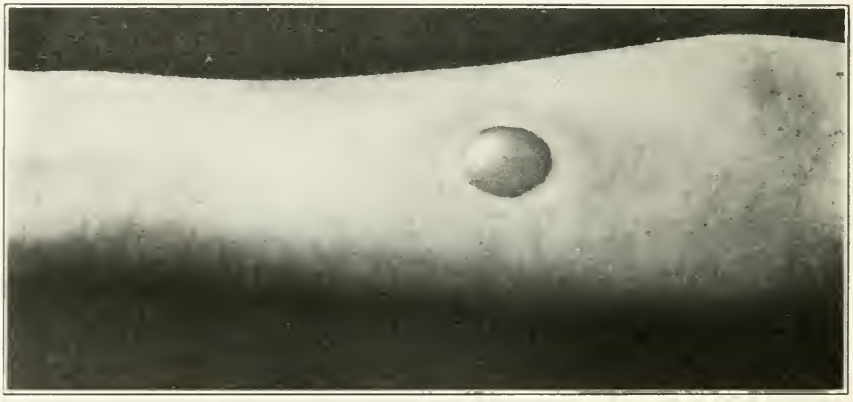

Fig. 8.—Lesion following the intradermal injection of 0.1 c.c. toxin (L + dose 0.18 c.c.) diluted 1 to 1,000. This and figure 7 illustrate the same case, different views. There are three well-defined zones—the vesicle, the anemic area surrounding it, and the pink areola.

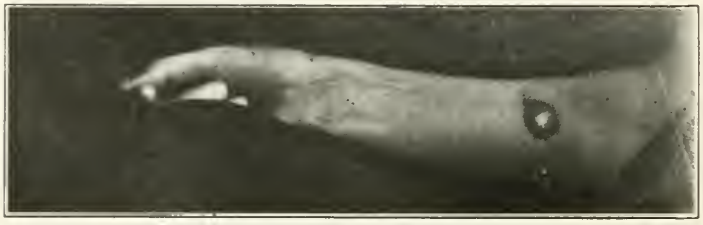

Fig. 9.—Lesion following the intradermal injection of 0.1 c.c. toxin (L + dose 0.18 c.c.) diluted 1 to 1,000.

TABLE 1.—Reactions Following Varying Strengths of Diphtheria Toxin Administered Intradermally

Date	Time After Injection	Site Number	Description of Reaction
4/12/16	12 hours	1	1 to 50,000. Faint hyperemia 13 × 17,* diffuse, flat
		2	1 to 40,000. Definite hyperemia 17 × 21, definite border, flat
		3	1 to 30,000. Definite hyperemia 15 × 22, pale red, definite border
		4	1 to 20,000. Marked hyperemia 17 × 18, light red, slightly elevated in center
		5	1 to 10,000. Marked hyperemia 20 × 25, red, definite border, slight elevation, pain on pressure
		6	1 to 5,000. Marked hyperemia 22 × 25, center deeper red, 5 × 7, elevated
4/13/16	24 hours	1	15 × 20, diffuse border, flat, pink.
		2	17 × 25, more definite border, flat; more hyperemic than 1
		3	22 × 27, more definite border, slightly more hyperemic than 2
		4	20 × 27, definite border, center slightly elevated, deeper pink, slight tenderness
		5	27 × 35, definite border, elevated slightly, not as much as 4, deeper pink, no tenderness
		6	28 × 35, border indefinite, same color as 5, darker pink zone at center, 5 × 5, slightly tender; slight edema. See Figure 2
4/14/16	2d day	1	10 × 10, pink tint, distinctly fading, flat, margin more definite
		2	15 × 15, pink tint, distinctly fading, flat, margin more definite
		3	15 × 15, pink tint, distinctly fading, flat, margin more definite
		4	15 × 15, pink tint, distinctly fading, deeper pink than 1, 2, 3, flat. Slight wrinkling
		5	20 × 23, deeper pink than 4, definite border, flat, pain on pressure, slight wrinkling
		6	20 × 30, slightly deeper pink than 5, definite border, flat, pain on pressure, slight wrinkling. The whole arm is slightly swollen and there is a slight pinkish hyperemic flush surrounding all the areas measuring 120 × 75
4/15/16	3d day	1	10 × 10, yellowish brown stain, not hyperemic
		2	10 × 15, fading, dull pink, slightly hyperemic, margin more diffuse
		3	10 × 15, fading but brighter than 2, hyperemic, flat, margin more diffuse
		4	15 × 15, fading but brighter than 3, hyperemic, flat, very slight wrinkling
		5	20 × 23, bright red, darker than previous day, hyperemic, flat, no soreness
		6	18 × 30, same as 5, flat. The general hyperemia described for 2d day has gone and the general swelling or edema of the forearm is distinctly less, but still noticeable, the veins are still obliterated
4/16/16	4th day	1	Almost gone, stain, which cannot be measured. The whole diffuse suggestion of discoloration was about 15 × 15
		2	10 × 15, just visible, brownish pink, no definite outline
		3	Seems smaller than 2, cannot measure, fading
		4	Fading, very finely wrinkled, about 15 × 15
		5	20 × 23, still dark pink, faded since 3d day, more dry on surface, wrinkled a little
		6	15 × 25, a little more marked than 5, no scaling, no marked wrinkling, general swelling less, veins still invisible

* Measurements are given in millimeters.

TABLE 1.—REACTIONS FOLLOWING VARYING STRENGTHS OF DIPHTHERIA TOXIN ADMINISTERED INTRADERMALLY—(*Continued*)

Date	Time After Injection	Site Number	Description of Reaction
4/17/16	5th day	..	All fading markedly
		1	Stain just seen
		2	10 × 15, fainter than 4th day
		3	10 × 10, fading, very diffuse border
		4	Same, a little more wrinkled
		5	Nearly the same, border less defined, wrinkled a little more
		6	Same, 15 × 25, deeper red than others, otherwise same as 5
4/18/16	6th day	..	All very much more faded
		1	2, 3 and 4 cannot be measured
		5	15 × 20
		6	15 × 25
		4	5 and 6 more wrinkled, no scaling yet
4/19/16	7th day	..	All fading much more
		1	Almost invisible
		5	and 6 scaling in large flakes
4/21/16	8th day	1	and 2, no scaling
		3	Faint
		4	5 and 6 marked

tion of a two-zone reaction; (2) the character of the periphery of the lesion; (3) the occurrence of scaling or desquamation; (4) the size of the reaction as influenced by the strength of the toxin; and (5) edema.

1. The Two-Zone Reaction: The statement is not infrequently made that a lesion with a dark center surrounded by a lighter pink areola, such as one so commonly sees in second intradermal injections of horse serum, should be looked on with suspicion as an indication of a pseudo or anaphylactic reaction. While doubtless a pseudo or protein reaction may occur with diluted diphtheria toxin, what I have termed a two-zone lesion does very frequently occur as a result of the action of the toxin itself. It is only a matter of either concentration, as is shown in Figures 1 to 6, or of individual tolerance, as is seen with the

TABLE 2.—Diphtheria Toxin 1 to 1,000 (L + D 0.18 C.c.) 0.1 C.c. Intradermally, Sept. 22, 1915

Case No.	Name	12 Hours	18 Hours	24 Hours	36 Hours	5 Days
1	Mr. B.*	7 × 9,† pale pink	10 × 10, red, elevated, definite border	15 × 15, faint pink, raised, margin red, center 2 × 3	.....	8 × 8, red area, no induration
2	Mr. H.	20 × 20, marked reaction, marked elevation, edema	20 × 25, same as at 12 hours	30 × 35, pale pink area, red center 15 × 15, border indefinite	20 × 20, pink fading	Fading
3	Mr. S. B.	7 × 8, very pale pink, no elevation	10 × 12, red definite border, elevated	12 × 12, same as at 18 hours	.....	Fading
4	Miss D.	17 × 22, red, elevated, definite border	23 × 25, same tint, border fading	35 × 35, elevated, indurated, border definite	25 × 25, red center, pink area	
5	Miss R.	11 × 12, deep red, definite border, slight elevation	10 × 10, pale pink border indefinite, slight elevation	18 × 28, deep red center 8 × 8, pink area, border definite, all elevated	10 × 10 vesicle area red and edematous	10 × 10, vesicle dry, area about it 5 mm. wide. Total area 15 × 15
6	Miss S.	17 × 22, deep red, marked elevation, border definite	23 × 35, same as at 12 hours	23 × 35, same as at 18 hours	Arm bandaged, definite blister formed	Arm bandaged, definite, blister formed
7	Mr. B.	10 × 13, pale pink, diffuse border	17 × 20, pale pink, definite border	.....	20 × 25, pink, fading	Blister 12 × 15, area about it 4 mm. wide, total area 15 × 19
8	Miss F.	18 × 22.....	.....	.....	50 × 70, red center, 20 × 22, area red	Vesicle said to have formed, not seen
9	Mr. O.	20 × 20, center elevated, hyperemia fades at border	40 × 30, pink with bright red center	40 × 30, same as at 18 hours	55 × 80, red, elevated center marked, border pink	10 × 10, pigmented rough area, desquamating
10	Mr. E.	22 × 30, bright red, marked elevation, border definite	28 × 30, same as at 12 hours			
11	Mr. G.	10 × 20, pink, flat, fading margin	.....	.....	30 × 40, slight edema, no vesicle	
12	Mr. Er.	10 × 15, pale pink, flat	14 × 15, pink, slightly elevated, border definite	14 × 15, same, but border less distinct	19 × 20, pink fading, no elevation	Negative
13	Miss S.	18 × 25, deep red, elevated, border definite	20 × 25, same as at 12 hours	30 × 35, bright red, margin raised	30 × 35, pink fading, no edema	Blister 20 × 30, 4 mm. high, area 45 × 60, white anemic band around vesicle 5 mm. wide. See figures 7 and 8

* Patient had 1,000 units of antitoxin subcutaneously.
† Measurements are given in millimeters.

standard Schick reaction (0.1 c.c. = $0.\dot{5}$ minimum lethal dose of toxin). This type of reaction is plainly seen in Figure 10. There is distinct edema in the center, and little or none at the periphery; necessarily there will be a difference in the color at these two places. A perfectly uniform color is probably more commonly seen than this two-zone reaction, however; even in some reactions that seem to be faint, careful observation will show not infrequently a darker central area surrounded by a lighter areola.

2. The Margin of the Lesion: The statement is sometimes made that the margin of the lesion must be well defined. This, too, depends

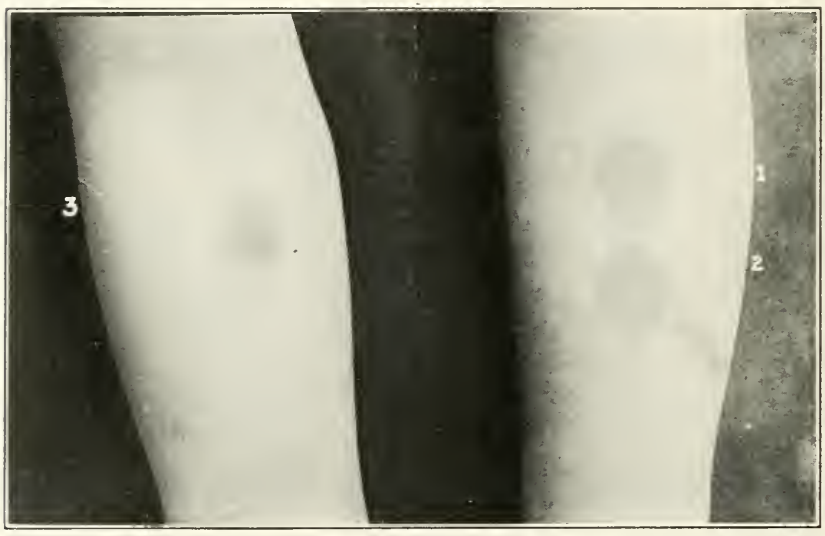

Fig. 10.—Madelain B., photograph taken March 28, 1916, eight days after the first intradermal injection: 1, first intradermal injection of 0.1 c.c., 1 to 20,000 dilution, on March 20; 2, second intradermal injection of 0.1 c.c., dilution 1 to 10,000, March 21; 3, third intradermal injection of 0.1 c.c., dilution 1 to 10,000, March 25. Nos. 1 and 2 are desquamating. Entire lesion elevated 1 mm. above surface, and has a leathery, thickened feeling. Total area at 3 is 18 × 25 mm., pink, central portion dark pink, slightly elevated, slight edema. The two zones are distinguishable.

largely on the strength of the solution and the susceptibility of the individual. In many of the reactions cited in this report, as well as in the series shown in Figures 1 to 6 and in Table 2, the statement, "diffuse border, the lesion cannot be measured, etc.," will be encountered frequently. We have had previous proof of a positive reaction in

some of these individuals, who now react less markedly because of a certain degree of immunity. This diffuse margin is well shown at sites 1 and 2, Figure 2. A definite impression of a typical reaction is here gained, but one could not definitely measure the lesion. It is very difficult to get a good photograph of a faint pink lesion. Many photographs of Schick tests show a measureable lesion with a definite border, when in fact beyond the area which seems fairly sharply defined is a gradually diminishing zone which fades almost imperceptibly into the color of the skin.

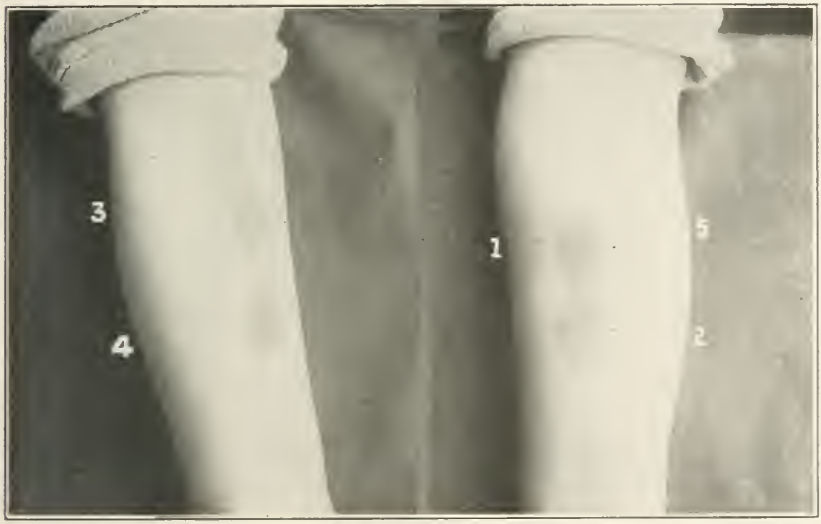

Fig. 11.—Madelain B., received on March 28, 1916, the fourth intradermal injection of 0.1 c.c. of toxin, and on April 11 the fifth injection of the same quantity on the left forearm just to the right of No. 1. The photograph was taken April 13. The age of each lesion on this date was as follows: 1, twenty-nine days; 2, thirty days; 3, nineteen days; 4, sixteen days, and 5, two days. This illustrates the diminishing reaction following successive injections No. 5, while 30 × 35 mm. was only a faint flush; the day following it was a light brown stain. Observe that lesions 1 and 2 are still very noticeable.

3. The Occurrence of Scaling: The typical lesion following the injection of 0.1 c.c. of Schick solution into a distinctly susceptible person almost, although not invariably, finishes up with characteristic scaling or desquamation, Figures 6, 10 and 12. As here shown, the lesion is often elevated well above the level of the skin. In less sus-

ceptible persons only a yellowish or brownish yellow stain remains, and this may vanish very quickly. This is well shown in the case recorded in Figure 11. This patient, after a degree of acquired immunity, gave no scaling at the point of the fifth injection. The same result, no scaling, was encountered many times in the series of successive injections.

4. The Size of the Reaction as Influenced by the Strength of the Solution: The average maximum size of lesions produced by different dilutions of the same lot of toxin is given as follows, the measurements

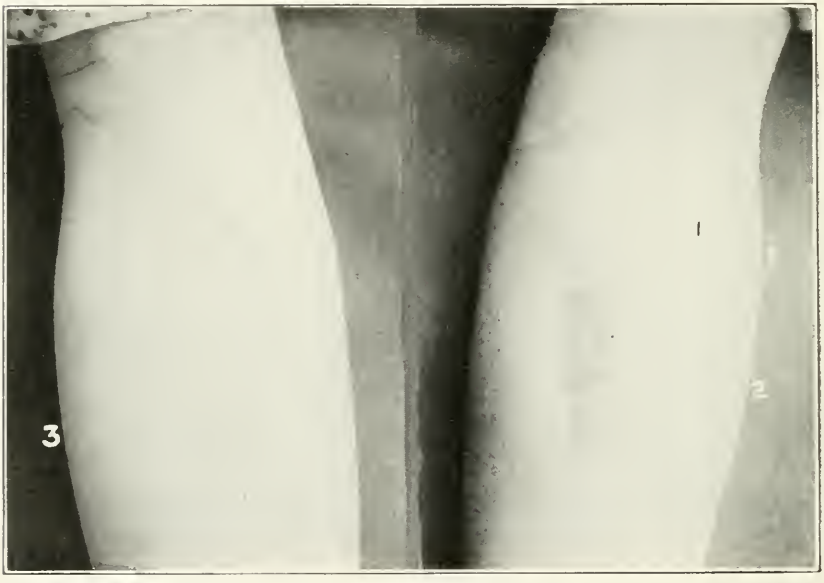

Fig. 12.—Loretta B., photograph taken March 28, 1916, eight days after the first injection, seven days after the second, and three days after the third. The effect of repeated injections is shown. This patient, like the one in Figure 11, continued to react positively after eight injections covering a period of over forty days. The reactions, however, are much modified, more superficial, and fade very much more quickly.

being taken from the fifty positive cases in the primary series of eighty-one cases:

Dilutions	No. of Cases	Average Maximum Reaction, Mm.	Amount Toxin, C.c.
1 to 20,000	10	10.9 × 15.1	0.000005
1 to 10,000	34	15.5 × 14.6	0.00001
1 to 1,000	13	27.4 × 34.6	0.0001

The reactions obtained with 1 to 20,000 and 1 to 10,000 solutions are the same, while those with the stronger solutions are very much greater in size.

The size of the reaction as influenced by the same dilution of different lots of toxin varies according to the strength of the toxin itself. No two lots of toxin are necessarily the same. On request, Parke, Davis & Co. of Detroit have kindly furnished me with the L + dose of five lots of diphtheria toxin taken at random, to which I add that of the lot used in making these tests, as follows: 0.5 c.c., 0.29 c.c., 0.25 c.c., 0.5 c.c., 0.29 c.c., 0.18 c.c. The L + dose of toxin used by Schick was 0.005 c.c.; accordingly, if one uses a standard-sized needle to deliver a definite amount of toxin into the skin, as has been recently advocated by Dr. Koplik, a definitely standardized toxin should be used. Susceptibility to diphtheria toxin, and consequently to diphtheria, can be recognized by very much more dilute solutions of toxin than are usually employed in making the Schick test.

The size of the reaction may be different with the same lot of toxin, the reason for which is hard to explain. For example, Mr. W. was given 0.1 c.c. of a 1 to 10,000 solution of Lot 1 and 0.1 c.c. of Lot 2. The lesion resulting from Lot 1 was very much more vigorous than that resulting from Lot 2, as will be seen in Table 3.

TABLE 3.—VARIATION OF REACTION DUE TO DIFFERENCE IN TOXINS

Toxin Lot	Ten Hours	End of First Day	End of Second Day	End of Third Day
1	+	20 × 20, deep pink, dark center 5 × 5 mm., elevated	10 × 11, deep pink, diffuse border, edema	7 × 8, fading pinkish, can't measure
2	0	15 × 15, fainter, flat	12 × 15, pink, red, flat, border diffuse	9 × 11, deep pink, flat, diffuse

Lot 1 happened to be an old solution, having stood many weeks. We would naturally expect this solution to deteriorate and give a weaker reaction than was obtained with the fresh solution, Lot 2. The solution was perfectly clear, however, and free from visible growth.

5. Edema: The intensity of the reaction, which seems to be indicated by the degree of redness and edema as well as by the size of the lesion, also depends on the strength of solution employed and the sus-

ceptibility of the person. In other words, there is no person the intensity of whose lesion cannot be varied at will by the choice of the strength of the solution injected. On the other hand, only those who possess little or no immunity react to the standard Schick solution with marked edema and induration. Such edema, for example, as can easily be seen and felt. Lesser degrees of edema, determined by pressing the lesion with the thin edge of the measuring rule or of the steel tape, are very commonly seen.

Reactions in Infants.—Intradermal tests were made on twenty-three infants, ages varying from 2 days to 10 months (ten positive, thirteen negative, or 56.5 per cent. negative). Negative reactions were encountered very frequently in infants under 5 months. No satisfactory explanation has been given for this immunity. It seems to have been a common clinical observation that young infants are seldom infected with diphtheria. Some authors go so far as to state that diphtheria never attacks an infant in the first half year of life, and believe this is due to a complete immunity. While my short series of cases seems to show that quite a large percentage of infants during this period of life are immune, there is still a large percentage who are not immune. This is rather in accord with the observations of Welch and Schamberg, who state that it has fallen to their "lot to see a large number of infants perish from this scourge (diphtheria) and many of them were under the age of 6 months." In their collection of 9,011 cases, 299, or 33 + per cent. were in infants under 1 year. Some observers, notably Schick, found only 7 per cent. of positively reacting cases in infants under 6 months. Similar results were obtained by Kassowitz and Gröer,[1] who report 10 to 20 per cent. positive. On the other hand, Kleinschmidt[2] found no antitoxin in sixteen out of eighteen infants examined.

It is sometimes very difficult to determine reactions of moderate degree in the newly born, because of erythema neonatorum, and particularly in some cases of icterus neonatorum, associated with erythema neonatorum. A very good light and a very careful observation is necessary, while in infants beyond the first two or three weeks of life the lesion is as easy to see as it is in a blond.

Family Reactions.—Park[3] and his co-workers have called atten-

1. Kassowitz and Gröer: Jahrb. f. Kinderh., 1913, lxxviii, 609.
2. Kleinschmidt: Jahrb. f. Kinderh., 1913, lxxviii, 442.

tion to the interesting point of family reactions; that is, if it is found that one member of a family of children reacts negatively or positively to a Schick test, all the rest of the children react in the same way. This observation has been confirmed by others. An early observation bearing on this point is that of Theobald Smith,[4] who in 1907 showed that conferred diphtheria immunity was transmitted to the offspring of guinea-pigs. It was further shown that this immunity remained active only over a period of thirty days, after which it gradually decreased until six months, when the offspring were no longer immune. This suggested to me the advisability of testing the mother and infant. The data obtained in this investigation are shown in Table 4.

TABLE 4.—RESULTS OF INTRADERMAL TEST APPLIED TO MOTHER AND CHILD

Number	Mother		Reaction in Infant	Age of Infant, Days
	Name	Reaction, Mm.		
1	West	15 × 15	Negative	10
2	Gray	20 × 21	Negative	9
3	Haynes	++20 × 25	Positive, 10 × 15	3
4	Prum	++20 × 25	Negative	2
5	Sweet	0	0	10
6	Bibbins	++30 × 30	0	3
7	McClure	++15 × 20	Positive +	4
8	Calhoun	++25 × 25	Positive +	6
9	Armstrong	++20 × 25	Positive ++	4

Table 4 shows that the mother and child were both positive in four instances, both negative in one instance, and mother positive and child negative in four instances. From these data it will be seen that while mother and child usually react in the same way, the infant may frequently give a negative reaction and the mother a positive. Kassowitz and Gröer believe the antitoxin is derived from the mother. The observations made above would lead one to believe that there are probably factors other than transmitted immunity entering into the negative reaction of the new born.

Influence of Time of Year on the Reaction.—It is a well-known

3. Park, Zingher and Serota: Arch. Pediat., 1914, p. 484.
4. Smith, Theobald: Jour. Med. Research, 1907, xi, 359.

clinical fact that diphtheria is more prevalent during certain seasons of the year. The U. S. Mortality Report for 1900, for example, records 16,368 deaths from diphtheria. Of these, 13,848 occurred during the cool and cold months, while 2,520, or about 15 per cent., occurred during the warm months, June, July and August. The influence of season on susceptibility of animals to diphtheria is well known, and has been recorded by Brown.[5] The guinea-pigs used in their experiments were more susceptible to diphtheria toxin mixtures in winter than in summer.

A great many toxin Schick reactions have been recorded in the literature, but, unfortunately, the time of year at which these reactions were made is frequently not given. One may infer, however, from

TABLE 5.—INFLUENCE OF SEASON ON SUSCEPTIBILITY TO DIPHTHERIA AS RECOGNIZED BY THE SCHICK TEST

Age	Summer				Winter				Reporter
	No. Cases	Pos.	Neg.	Per Cent. Pos.	No. Cases	Pos.	Neg.	Per Cent. Pos.	
Under 1 year...	20	6	14	30*	48	16	32	33.3	Moffett and Conrad*
One year.....	27	9	18	33.3*	36	20	16	55.5	Moody†
One to 5 years.	..	..	..	....	24	21	3	87.5	Author
Totals.....	47	15	32	31	131	66	65	58	

* Moffett and Conrad: Jour. Am. Med. Assn., lxv, 1010.
† Moody: Jour. Am. Med. Assn., lxiv, 1206.

the date of publication and from the context the time of year at which the test was made. The cases recorded in Table 5 are, I believe, trustworthy as to season. The figures are only suggestive. It is not at all improbable, however, that it will be found that more negative reactions will be encountered in the warm summer months than in winter.

PART II

SUCCESSIVE INJECTION SERIES

Of thirty-four positive cases in which successive intradermal injections of toxin were given (Table 6) at intervals of five, twelve and seven days, respectively, the time of the reaction was unchanged in

5. Brown: Jour. Med. Research, 1912-1913, xxii, 447.

nine cases, hastened in twenty cases, delayed in no instance, and completely suppressed in five instances. The character of the reaction was unchanged in five cases, diminished in twenty-four cases, and suppressed in five cases.

Suppressed Reactions.—The suppressed reactions seem to have been brought about definitely by the repeated injection of toxin. All of these cases gave small but nevertheless distinct primary reactions. In two cases the primary reactions were delayed. The suppression was induced by the first injection of toxin.

The Hastened Reactions.—Of the twenty cases in which the time of the appearance of the reaction was hastened by successive injections of toxin, a primary reaction occurred on the second day in eight cases, on the third day in six cases, on the fourth day in six cases.

Of the eight cases reacting on the second day, the hastening of the time of the reaction was effected by the first injection in four cases, by the second injection in four cases.

Of the six cases reacting on the third day, the hastening of the time of the reaction was effected by the first injection in five cases, by the second injection in one case.

Of the six cases reacting on the fourth day, the hastening of the time of the reaction was effected on the first day in four cases, on the second day in one case.

From this observation it seems that the hastening of the time of the reaction is usually effected by the first injection, that is, a delayed primary reaction case through the influence of the first injection responds more quickly to a second injection after an interval of five days.

While analogous to the phenomena seen after second injections of horse serum, this change in reactivity is not an anaphylactic affair. It is in all probability due to an acquired immunity.

The Diminishing Reactions.—Twenty-four of the positively reacting cases showed a diminution in the size and the intensity of the reaction. This was very noticeable in twelve cases (Cases 3, 9, 11, 16, 22, 28, 29, 30, 32, 33, 45, 52, Table 6). The time of the first appearance of the reaction was hastened in sixteen of these cases, unchanged in eight, but in the latter, seven reacted primarily on the first day. In those cases in which the primary reaction occurred on the fourth day the reaction was so slight after the second injection (which was given five days later) as to be marked "+—" in two (Cases 11, 57,

TABLE 6.—Successive Intradermal Injections in Positive Cases

Case Number	1st Injection, Dilution 1 to 10,000		2d Injection, 5 Days after 1st, Dilution 1 to 10,000		3d Injection, 17 Days after 1st, Dilution 1 to 5,000		4th Injection, 29 Days after 1st, Dilution 1 to 10,000		5th Injection, 36 Days after 1st, Dilution 1 to 20,000		Influence of Successive Injections	
	Maximum Reaction, Mm.†	Day 1st Reaction	Maximum Reaction, Mm.	Day 1st Reaction	Maximum Reaction, Mm.	Day 1st Reaction	Maximum Reaction, Mm.	Day 1st Reaction	Maximum Reaction, Mm.	Day 1st Reaction	On Time of Reaction	On Character of Reaction, Size, Intensity, etc.
1*	+	2	+	2	.....	...	.....	...	.....	...	Unchanged	Unchanged
2*	7 × 7	3	8 × 10	1	8 × 8	2	10 × 17	1	6 × 7	1	Hastened	Diminished
3*	15 × 22	3	4 × 5	1	10 × 17	1	.....	...	.....	...	Hastened	Diminished
7*	10 × 15^3	1	13 × 18^2	1	12 × 15^2	1	10 × 15	2	8 × 10	1	Unchanged	Diminished
9*	15 × 17	4	15 × 18^4	3	6 × 8	2	±	1	7 × 8	1	Hastened	Diminished
11*	8 × 10	4	±	2	.....	...	.....	...	.....	...	Hastened	Diminished
16	10 × 20	3	3 × 7	1	.....	...	.....	...	.....	...	Hastened	Diminished
17	12 × 12^3	2	20 × 20^3	1	.....	...	.....	...	8 × 10	1	Hastened	Diminished
18	15 × 15^5	2	7 × 10	1	9 × 6^2	1	5 × 5	1	7 × 10	1	Hastened	Diminished
19	10 × 10^3	1	8 × 10	1	12 × 17^4	1	6 × 8	1	10 × 12^2	1	Unchanged	Diminished
20	7 × 10^3	3	0	0	.....	...	.....	...	.....	...	Suppressed	Suppressed
21	8 × 10	2	10 × 14^4	2	7 × 7	1	6 × 9	1	12 × 12	1	Hastened	Diminished
22	10 × 13	1	5 × 3	1	.....	...	5 × 6	1	5 × 8	1	Unchanged	Diminished
23	8 × 8	3	11 × 11^2	1	.....	...	.....	...	8 × 10	1	Hastened	Unchanged

24	10×12	3	15×15	3	.....	...	7×7	1	8×10	1	Hastened	Diminished
25	$\pm$	4	4×4^4	1	.....	...	.....	...	.....	...	Hastened	Unchanged
26	15×15	1	5×5^2	1	.....	...	10×13	1	12×12	1	Unchanged	Diminished
27	18×20^4	2	8×15^3	1	8×10^2	1	8×12	1	8×10	1	Hastened	Diminished
28	12×15^4	2	2×2	1	.....	...	.....	...	.....	...	Hastened	Diminished
29	17×20^2	2	+	1	.....	...	.....	...	.....	...	Unchanged	Diminished
30	10×18^3	1	10×16^3	2?	8×7^2	1	.....	...	.....	...	Unchanged	Diminished
32	12×15	3	+	1	.....	...	.....	...	.....	...	Hastened	Diminished
33	8×10	4	+	2	.....	...	.....	...	.....	...	Hastened	Diminished
36	+	1	0	0	.....	...	.....	...	.....	...	Suppressed	Suppressed
39	10×15	4	10×10	3	.....	...	.....	...	.....	...	Hastened	Unchanged
45	12×20^3	2	16×20	2	5×7	1	.....	...	.....	...	Hastened	Diminished
46	18×22	2	19×20	2?	16×17	2	.....	...	.....	...	Unchanged	Diminished
52	15×20^2	1	8×8^4	1	.....	...	.....	...	.....	...	Unchanged	Diminished
53	12×15^3	2	10×10^4	2?	10×17^2	1	8×5	1	8×10	1	Hastened	Diminished
54	3×5^2	3	0	0	.....	...	.....	...	.....	...	Suppressed	Suppressed
56	$\pm$	1	0	...	.....	...	.....	...	.....	...	Suppressed	Suppressed
57	5×8	4	$\pm$	2	.....	...	.....	...	.....	...	Hastened	Diminished
59	5×8	4	0	0	.....	...	.....	...	.....	...	Suppressed	Suppressed
61	10×12^3	2	10×10	2	10×13	1?	.....	...	.....	...	Hastened	Unchanged

* The patients in Cases 1, 2, 3, 7, 9 and 11 received for the first injection a dilution of 1 to 20,000.
† In the maximum reaction column the exponent indicates the day on which the maximum reaction occurred.

Table 6), and "+" in 1 (Case 33). In other words, it was a question whether there was a reaction at all in two cases, with the benefit of the doubt given to the positive side.

The successive changes which occur in the diminishing group of reactions will be appreciated better by referring to Tables 7 to 11, which give the daily measurements, etc. These tables are self-explanatory.

The question of delayed appearance of primary reactions referred to in the first part of this report seems to be of some significance. In quite a number of the suppressed and diminishing reaction cases the change consequent on repeated injections of toxin to negative or slight reactions is quite noticeable in the late primary cases. From this, one might infer that individuals reacting to a primary injection of diphtheria toxin on the first day have less immunity than those reacting on the third and fourth day. In other words, a delayed reaction means that the individual has a certain amount of immunity, and will, in all probability, be a case which would more readily become immunized by injection of toxin or toxin-antitoxin mixtures.

The Unchanged Reactions.—Those cases in which the character of the reaction was unchanged are four in number (Cases 1, 23, 25 and 61, Table 6). Two of these cases (1 and 25) were of slight reaction, and the patients passed from under observation after the second injection. The other two (23 and 61) were apparently uninfluenced by repeated injections. In Case 23 the patient missed the third and fourth injections, thus leaving a period of thirty days between injections. This case, however, showed reaction within the first twenty-four hours, while the reaction did not appear until the third day after the first injection.

Negatively Reacting Cases.—Of the patients reacting negatively to successive injections of diphtheria toxin, sixteen remained in the hospital long enough for a second and third injection, given at intervals of five, twelve and fourteen days. Fourteen of these remained negative, while two gave slightly positive reactions after the second injection. These must be considered variants. Case 58 may have been positive after the primary injection, we marked it "— ?," while Case 15, on the other hand, followed the usual distinctly negative course. The reactions were carefully watched over periods of from five to seven days.

This negative group, together with the diminishing positive group,

TABLE 7.—CASE 9, CLARENCE Y., AGE 11 YEARS*

Inj. No.	Date of Injection	Dilution of Toxin	Reaction in Mm.						
			1st Day	2d Day	3d Day	4th Day	5th Day	6th Day	7th Day
1	11/ 7/14	1 to 10,000	0	0	0	15 × 17, red	15 × 17, fading	Fading	Fading
2	11/12/14	1 to 10,000	0	0	±	15 × 18, faint	Fading	Fading	Fading
3	11/24/14	1 to 5,000	+ ?	6 × 8	..	Fading	Fading	Fading	Fading
4	12/ 6/14	1 to 10,000	±	Fading	0	0	0	0	0
5	12/12/14	1 to 10,000	7 × 8	Fading	0	0	0	0	0

* This case illustrates the hastened and diminishing reaction.

TABLE 8.—CASE 18, BABY W.

Inj. No.	Date of Injection	Dilution of Toxin	Reaction in Mm.						
			1st Day	2d Day	3d Day	4th Day	5th Day	6th Day	7th Day
1	11/ 7/14	1 to 10,000	?	++	++	12 × 12	15 × 15,	Fading	Fading
2	11/12/14	1 to 10,000	7 × 10	+ papule	+	+	Fading	Fading	Fading
3	11/24/14	1 to 5,000	5 × 7, bright red	6 × 9	....	Fading	Fading	Fading	
4	12/ 6/14	1 to 10,000	5 × 5	8 × 8, stain	0	0	0		
5	12/12/14	1 to 20,000	7 × 10	Fading quickly	Stain	—	—		

TABLE 9.—CASE 22, BABY R.

Inj. No.	Date of Injection	Dilution of Toxin	Reaction in Mm.						
			1st Day	2d Day	3d Day	4th Day	5th Day	6th Day	7th Day
1	11/ 7/14	1 to 10,000	10 × 13	10 × 12, red	8 × 9, fading	Fading	Fading	Fading	Fading
2	11/12/14	1 to 10,000	5 × 3	+	+	Stain	Fading	0	
3	11/24/14	1 to 5,000	5 × 7	8 × 8	....	Left hospital			
4	12/ 6/14	1 to 10,000	5 × 6	5 × 6	0	0	0	Returned to hosp.	
5	12/12/14	1 to 20,000	5 × 8	Fading	0	0	0		

TABLE 10.—CASE 45, GENEVIEVE H.

Inj. No.	Date of Injection	Dilution of Toxin	Reaction in Mm.						
			1st Day	2d Day	3d Day	4th Day	5th Day	6th Day	7th Day
1	11/ 7/14	1 to 10,000	0	+	12 × 20	Fading	Fading	Fading	Fading
2	11/12/14	1 to 10,000	....	16 × 20	16 × 20	17 × 20, fading, general rash*	Fading	Fading	Fading
3	11/24/14	1 to 5,000	5 × 7, faint	8 × 8 ?, faint	Left hosp.				

* On Nov. 16, 1914, nine days after the first injection and four days after the second, the patient broke out with a general erythematous eruption, macular in character. This was most noticeable on the right side of the face, where there was a map-like area 7 by 7 cm. There were several large areas on the chest and abdomen 5 by 5 cm. and a few on the arms 2 by 2 cm. The color was deep red. The lips and the lower eyelids were swollen. The cervical glands on the left side were enlarged, but no previous note had been made of their condition prior to injection.

TABLE 11.—CASE 30, ZENA B.

Inj. No.	Date of Injection	Dilution of Toxin	Reaction in Mm.						
			1st Day	2d Day	3d Day	4th Day	5th Day	6th Day	7th Day
1	11/ 7/14	1 to 10,000	6 × 13	±	10 × 18	12 × 18	Fading, yellow	Yellow	Fading
2	11/12/14	1 to 10,000	....	8 × 8	+ not measured	10 × 16, fading	Fading	Fading	Fading
3	11/24/14	1 to 5,000	6 × 7	7 × 8, faint	+ not measured	Fading	Fading	Fading	

confirms the opinion that toxin even in these minute amounts tends to stimulate the formation of antitoxin, rather than to use up to any appreciable degree the natural antibodies of the organism.

To carry the investigation a little farther, three children with marked reactions to a 1 to 10,000 solution of toxin were selected, an intradermal injection of the same amount of toxin being given at the intervals of one, four, three, fourteen, fifteen, ten and three days, covering a period of forty days. On one day, April 11, 1916, at the time of the fifth injection, 0.2 c.c. of this solution was also injected into the thigh of each child as a control. The noticeable thing about these reactions is that although the children do not react negatively after the repeated injections, the lesion has been definitely modified. Though it has not become smaller, its duration is much shorter, and in a few days

after an injection of toxin, the fourth or fifth day, the stain is the same or less noticeable than it is in the first or second lesion. It is a well-known fact in the manufacture of diphtheria toxin that horses develop a very high-grade local immunity in the tissues surrounding the point of injection of the toxin, and a low-grade general immunity.[6] This is shown by the development of well-marked local necrosis when the same dose of toxin is injected into a remote part of the skin. To guard against this having any influence on the reactions recorded, the injections were made into both arms, and test injections were made into other parts of the skin, such as the thigh, for a control. The changes that have been induced by the successive injections, I believe, are not due to a local skin change. The total amount of toxin used in each of the last three cases was 0.0001 c.c. (minimum lethal dose 0.0015).

It has been shown that repeated doses of diphtheria toxin induce immunity in guinea-pigs, but that such immunity does not compare with that induced by toxin-antitoxin mixtures. When toxin alone was used, doses of toxin which were not large enough to produce skin lesions (necrosis and ulceration) were selected. The first doses (Brown[7]) used produced only slight scaling of the skin and little loss of hair. The offspring from such treated mothers showed a resistance to toxin above normal. Amounts of toxin varying from 0.0023 to 0.0098 c.c. (minimum lethal dose 0.007) were injected. Immunity was developed to the point that no local or constitutional reaction was produced by 0.005 c.c. of the toxin. With children, solutions of greater than 1 to 5,000 concentration of our toxin brought about ugly lesions when injected intracutaneously.

The Occurrence of Rashes Following Intradermal Injections of Diphtheria Toxin.—Rashes were observed in five cases, Ula S., Baby G,. Genevieve H., Sarah S. and Loretta B. All of these rashes developed after the second injection, and all appeared on the second or third day after this injection was given. These rashes were erythema in four and urticaria in two. That the rashes were due to repeated injection of toxin is well seen in the cases of Loretta B. and Sarah S. In Loretta B. marked erythematous and urticarial patches appeared on the face, 10 by 25 mm., and on the back, 20 by 30 mm., on three different occasions, always the beginning of the second day after an

6. Smith and Brown: Jour. Med. Research, 1910, xviii, 443.
7. Brown: Jour. Med. Research, 1912-1913, xxii, 445.

injection. In Sarah S. the urticaria was very marked, extending over the entire body, and persisting for several days. This occurred on two occasions. Cases showing erythema resembled that shown in Genevieve H., but they were not so marked. Genevieve H. developed a macular erythema, beginning the night of the second day following her second intradermal injection, nine days after her first injection. The eruption extended over the entire body, and was most noticeable on the right side of the face, where a large map-like area, 7 by 7 cm. developed. Several large areas developed on the abdomen, 5 by 5 cm., and several on the arms, measuring 2 by 2 cm. The color was a deep red, and the lips and the lower eyelids were swollen. The posterior cervical glands were enlarged on the left side, but no record of their previous condition had been made. These children had never had similar rashes before.

SUMMARY

It would seem from the foregoing observations that the following conclusions are justified:

1. Successive intradermal injections of very dilute solutions of diphtheria toxin (0.00001 c.c. L. + dose), when given at intervals varying from five to twelve days, provoke the formation of antibodies, and in those cases already exhibiting a certain degree of immunity, bring about a definite immunity as recognized by the intradermal test.

2. An opinion of the degree of natural immunity may be obtained from the time of first appearance and from the character of the primary intradermal reaction. An early primary reaction of ordinary degree indicates absence, or low degree, of immunity. A late appearing primary reaction indicates that such a person has a greater degree of immunity than one who reacts early.

3. The development of immunity induced by means of infinitesimally small successive doses of diphtheria toxin may be recognized by a hastening in the time of the appearance of the reaction, and a diminishing of the size of the lesion.

4. In those cases in which the size and intensity of the reaction was reduced by successive injections of toxin, the time of the appearance of the reaction was hastened in the large majority of cases observed. The greatest change toward a negative reaction occurred in those cases which gave a primary reaction on the third and fourth day.

5. A primary reacting case which does not change its character

after a second, third or fourth intradermal injection may be considered one without any reacting bodies, and, necessarily, one in which diphtheria would be easily induced.

6. The degree of immunity induced by such small doses of toxin as are represented by 0.1 c.c. of highly diluted diphtheria toxin, seems to be very slight, and cannot be compared with the results obtained by the use of toxin-antitoxin mixtures. Solutions carrying sufficient toxin to induce immunity when given intradermally are not well borne by the patient.

I wish to acknowledge the kind assistance of Dr. A. H. Beifeld in confirming many of the measurements and observations made.

DISCUSSION

DR. KOPLIK: There are two points brought out by Dr. Cowie that I think should be emphasized. The first is the standardizing of the particular preparation of diphtheria toxin; because manufacturers who are furnishing this substance to experimenters supply a toxin that differs materially from the standardized solution used by the New York board of health, which directs the intradermic injection of one-fiftieth of the lethal dose for a guinea-pig. In this paper the toxin is twice as strong as this, so it may be that the different results obtained in the skin test varied on this account.

The other point is the anaphylactic pseudoreaction. In all reactions, whether anaphylactic or positive, a certain amount of the reaction is due to trauma. In pseudoreactions the discussion has been very rife as to whether most of the reaction of the pseudoreaction may not be due to traumatism, and the vanishing amount in the true reaction due to the toxin. Dr. Unger and myself used a definite amount of toxin of a standardized solution, injecting it into the skin. There is a minimal amount of trauma when this method is employed, and the children do not seem to object to it. We have succeeded in practically eliminating pseudoreactions, for this reason: In every test we made we inoculated the right arm with the board of health solution, according to the method of Schick; and the left arm, with our own. We found a difference in the same individual. We discovered that we could eliminate the pseudoreactions and anaphylactic reactions of the toxin, and obtain either a positive or a negative true reaction. In the Schick method the large area of the lesion obtained may also be due partly to traumatism, and in the new method, in which the needle is dipped in the solution and then passed into the skin, the reactions are smaller than in the classical Schick reaction.

I wished to call attention to these points. These photographs confirm our own work, especially the blistering that takes place, in some cases is very extreme. In one or two cases we had to dress the wound.

DR. HESS: In this procedure, both the Schick test and the toxin-antitoxin mixture are especially adapted to children in an institution, rather than those in a hospital. In the institution with which I am connected, for the past two years we have used the Schick test a great many times on the 400 inmates. During the past year the children who gave a positive Schick test received the toxin-antitoxin mixture.

There is one point that I think should be emphasized. If these toxin-antitoxin mixtures confer immunity in every case, we should consider our institution to be at present immune from diphtheria, because every child with a positive Schick test received the toxin-antitoxin mixture. For a while we thought that this would be the case, but presently there developed a case that I think is instructive. It was one of laryngeal diphtheria with diphtheria bacilli on culture, and a postmortem examination showed diphtheria in the trachea and a membrane, both macroscopic and microscopic, on the larynx. This merely means, not that the mixture was of no value, but that it does not bring about an active immunization in all cases. When one injection of toxin-antitoxin is given, a certain amount of immunity is conferred in perhaps from 50 to 60 per cent. of the cases. When two injections are given, as in this case, about 15 per cent. of the children develop no immunity, and this child was evidently one of that small percentage who are unable to form antitoxin. It is the same with horses, and there exist many means between these two extremes.

A. MEASLES, PERTUSSIS, TEMPORARY CHEST DEFORMITY; *B.* PERTUSSIS; *C.* PERTUSSIS, MEASLES, PNEUMONIA

A GROUP OF CASES OCCURRING SIMULTANEOUSLY IN ONE FAMILY

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A. On Feb. 2, 1916, we were called to see a little girl, Margaret G., 9½ years old, who had had a rather severe cold, with harsh cough, for a few days. On examination we found a characteristic throat, Koplik spots, a conjunctivitis, and the beginning of a measles rash behind the ears, on the cheeks, and on the neck. The temperature was 101.6. On February 3 the patient was well covered with typical rash, but the cough was less severe. On February 4 the mother reported that the cough had been more severe during the night, and she thought the child had whooped once. The mother was on the watch for this development, as the other children, as will be later noted, were about half way through an attack of pertussis. The patient was at once put on bromoform, and the dose ordered increased a drop daily. On the 7th she was coughing pretty hard. She had had a little earache the night before, but a 5 per cent. solution of pure phenol (carbolic acid) in chemically pure glycerol took care of this trouble. On the 8th the paroxysms of coughing being severe, though not unduly frequent, pertussis vaccine was given, and was repeated in increasing doses on the 10th and 12th. The bromoform was also increased, as the child began to complain of soreness in her chest wall. On the 12th we noted that all traces of the measles had gone, and that the child was much better, and this improvement, even to the cough, continued. Again, on the 18th or 19th the child complained of the discomfort of even the few paroxysms of coughing with which she was still troubled, and was instructed to wear a tight 6-inch belt of canton flannel around the chest, covering the surface from the nipple lines, horizontally, downward. Examination at this time showed a bulging of the lower chest wall, more marked on the left, and a seeming dislocation of the anterior parts of the lower attached ribs to their cartilages. The malposition could be easily reduced by pressure of the hands, and apparently no function of other parts was interfered with. Under increasing doses of bromoform, the cough rather quickly ended, and by the end of the month the child had only an occasional paroxysm of coughing with no whooping and had begun to improve in color, appetite, and weight. Her chest deformity diminished slowly, and she is now in almost normal condition in every way, though there is still a little deformity on the left side.

Just a word as to her treatment. The measles was treated by the exhibition of plenty of cool, fresh air, night and day, and the patient occasionally had a simple cough mixture, up to the time the bromoform was started. This latter remedy was pushed to the point of fair control of the disease, and as rapidly as possible. The first injection of vaccine contained four hundred and thirty millions, the second, eight hundred and sixty millions, and the third,

twelve hundred and ninety millions. Saccharated iron was the tonic used subsequent to the bromoform, and seemed to be efficient in building up her hemoglobin.

B. On Feb. 2, 1916, while visiting the patient whose record has just been given, we heard some most violent paroxysms of coughing, accompanied with very marked whoops. On going into the next room, we found this patient, aged 5 years, and his brother, aged 2 years, coughing and whooping violently. They had had this type of cough at least ten days, and no treatment had been given. Both patients were put on bromoform in increasing doses, and the response of this patient, James, was very prompt. His cough soon became less frequent and less severe, but because of the exposure to measles, the child was given two injections of vaccine, about two hundred and seventy-five and five hundred and fifty millions respectively. He was daily examined for measles signs, but developed none, and soon was well. The bromoform was diminished in about the same way as it was increased, until the patient was fully recovered. Shortly after he was pronounced well, he had some rheumatic pains in the joints of his legs and arms, which promptly disappeared under aspirin. He has remained well up to the present time.

C. As has been related, the 2-year-old, Paul, was suffering on February 2 from a severe attack of pertussis. The bromoform was increased as rapidly as possible, just keeping him on the verge of drowsiness. Because we were expecting measles in his case, and because he was not robust, we gave him three doses of vaccine of one hundred and seventy, three hundred and forty, and five hundred and ten millions respectively, to mitigate, as far as possible, the dangers which might come from a later combination of pertussis and measles. He responded to the treatment very well, but on February 12 he was well broken out with typical measles, and the measles cough was added to that of pertussis. Much trouble also was experienced from accumulations of gas in the abdomen, relieved promptly, as a rule, by enemas of glycerol and water. By the 19th the rash had faded, but the child was stupid, looked toxic, and the chest was full of fine râles. On the 20th he looked and acted as if he had a pneumonia, but no physical signs could be elicited. The pulse was good. The child was repeatedly examined by us both for signs of consolidation, but none were found. During the evening of the 21st the mother thought the child was better, gave him an enema during the evening, because he was a little uncomfortable from the abdominal distention, and about midnight lay down beside him, as the child was sleeping quietly. Some time later she awoke and found the child apparently not breathing. I arrived soon after, but the child was dead. I at once percussed the chest and found a small area of dulness at the left apex, possibly confirmatory of our idea that a pneumonia was present or developing.

These cases are presented to show how a double infection in one family may work out. The pertussis was probably brought home from kindergarten by the 5-year-old, James, but Paul probably got his infection about the same time, as the school building is within 150 feet of the house, and several hundred children pass the door each school day. Margaret probably contracted pertussis from her brothers, infecting them in turn with measles, which she undoubtedly picked up at school, measles having been epidemic in Pittsburgh since before New Year's.

It is much to be regretted that a roentgenogram was not taken of Margaret's chest, but she could not be taken from the premises, and the weather was so cloudy and stormy that an ordinary photograph taken in the house would have been useless.

We also wish to point out that, although Mulford's pertussis serobacterin mixed, containing pneumococci, was used three times with the 2-year-old, he most probably had a pneumonia.

OBSERVATIONS ON MEASLES

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The deaths reported as due to measles give a very inadequate and incorrect idea of the real number due to this disease, for it is well known that most of the deaths are not due to the original disease, but to a complicating bronchopneumonia, and many physicians who have failed to report the original disease do not mention it on the death certificate. Most of these deaths occur in patients between 1 and 2 years of age. Chart 1 shows the curve of morbidity from measles in New York City during 1915, and the curve of mortality from bronchopneumonia in children between 1 and 2 years during the same time. It will be seen that these curves run nearly parallel, which, although not conclusive, is at least suggestive. It may be objected that the curves of other communicable diseases would show the same parallelism; I have therefore added those of scarlet fever and diphtheria. It will be noted that they do not show the sudden rise and fall.

However, measles is an important disease, not only on account of its complications and deaths, but also because it probably offers the best opportunity for studying the problems of infection, incubation and immunity. The infection takes place with such certainty, the duration of the period of incubation is so uniform, and immunity is conferred so regularly. As it is a very common disease, in epidemics one often has an opportunity of studying a very large number of cases.

In the short time at my disposal I shall discuss briefly a few observations more or less disconnected. Table 1 is based on a series of 300 secondary cases and shows the number of days that elapsed between the time of infection and the appearance of fever, catarrh, tonsillar spots, Koplik spots, and the eruption. For the sake of simplicity the numbers have been reduced to percentages. It will be seen that fever was the earliest symptom and appeared most frequently on the tenth or eleventh day (56 per cent.), the catarrhal manifestations most frequently on the eleventh or twelfth day (60 per cent.), the tonsillar spots appeared with nearly equal frequency on the ninth, tenth, eleventh, twelfth and thirteenth day, the Koplik spots were

most frequently seen on the eleventh and twelfth day (54 per cent.), and the eruption appeared most frequently on the twelfth, thirteenth or fourteenth day (67 per cent.). The catarrh was present in 7.2

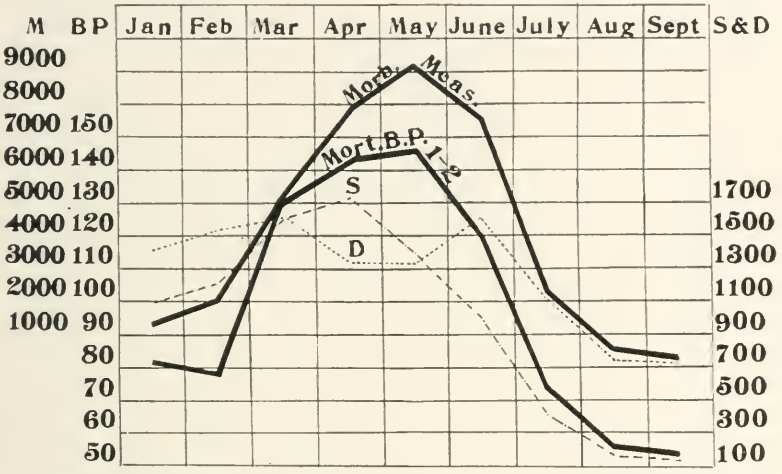

Chart 1.—New York City, 1915. Showing the parallelism between the curves of morbidity from measles and mortality from bronchopneumonia in infants between 1 and 2 years of age. The curves of morbidity from diphtheria, D. and scarlet fever, S. do not show this parallelism.

Day	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Fever	4.	6.3	13	33	23	7.6	6.3	4.3	1.	.6				
Catarrh	.4	.7	4.7	14	34	26	9.8	5.	1.5	2.5	1.1		.3	.3
Ton. sp.	4		14	16	25	22	18							
Koplik			2.8	10	28	26	18	7.4	2.3	2.8	.9		.5	.5
Erupt.				1.5	6.	18	29	20	13	6.	3.5	1.5	.3	.3

TABLE 1

Based on 300 secondary cases of measles. Showing number of days that elapsed between the time of infection and the appearance of fever, catarrh, tonsillar manifestations, Koplik spots, and the eruption. Given in percentages of cases.

per cent. on or before the tenth day, the Koplik spots in 12.3 per cent. and the tonsillar spots in 34 per cent. The tonsillar spots have been seen more regularly in the more recent cases, probably because they

were looked for earlier. It will be noted that in 4 per cent. of the cases in which they were present they were seen as early as the seventh day, at a time when there was nothing but a slight rise of temperature to indicate that the child was not well. In a few cases the tonsillar spots were present in patients who did not show any Koplik spots. Although their presence is not absolutely pathognomonic, their value is very great in hospitals, asylums and schools, because it makes it possible to detect and isolate secondary cases early.

Infants under 2 months of age are absolutely immune. As they grow older this immunity becomes less absolute, so that at eight months it is apparently entirely lost. This gradual disappearance can be demonstrated in various ways. Table 2 shows the number of days which elapsed from the time of infection to the appearance of the eruption. Of the 300 patients sixty-three were under 8 months. Of these none were under 4 months and only four were under 5 months. It will be seen that in 81.4 per cent. of those over 8 months the eruption appeared on or before the fourteenth day, whereas in only 42.5 per cent. of those under 8 months did it appear at that time. This prolonged incubation period would tend to indicate a relative immunity in infants under 8 months. The same is indicated in another way. In infants between 5 and 8 months of age the disease is usually milder and the appetite is not entirely lost. I was able to obtain the weights of 59 patients under 2 years at the time of exposure to infection and at the onset of the disease. Of these seventeen were under 8 months and forty-two were between 8 months and 2 years. Of the young infants only seven (41 per cent.) showed a loss in weight, whereas of the older children thirty-two (76 per cent.) lost in weight.

The immunity enjoyed by young infants is not conveyed through the breast milk, for I have found that artificially fed infants are also immune. It seems most likely that it is conveyed through the placental circulation, and this would account for its gradual disappearance. It is also an interesting fact, that only in places in which measles is endemic do the infants enjoy such immunity. For example, in New York City practically every child is exposed to the infection at home or in school before it reaches the age of 10, so that it is exceedingly rare to find a mother who has not had measles. On the other hand, in certain isolated islands of the Pacific Ocean the disease breaks out only at long intervals, so that it is possible for a mother to have children, without having herself been exposed to infection. These children

are not immune. This difference in the prevalence of the disease in different localities may possibly account for the apparent differences of opinion among authors as to the frequency of measles in children under 5 months of age.

It is an interesting fact that when infants between 3 and 5 months of age are exposed to infection and do not contract the disease, they

Day Erupt.	10	11	12	13	14	15	16	17	18	19	20	21
Over 8mos	1.5	6.3	20	31	23	11	4	2.2	.7	.7		
Under ,,		4.7	9.5	22	6.3	24	14	9.5	4.7	1.6	1.6	1.6

TABLE 2

Showing the number of days that elapsed between the time of infection and the appearance of the eruption in the patients under, as compared with those over, 8 months of age. Given in percentages of cases.

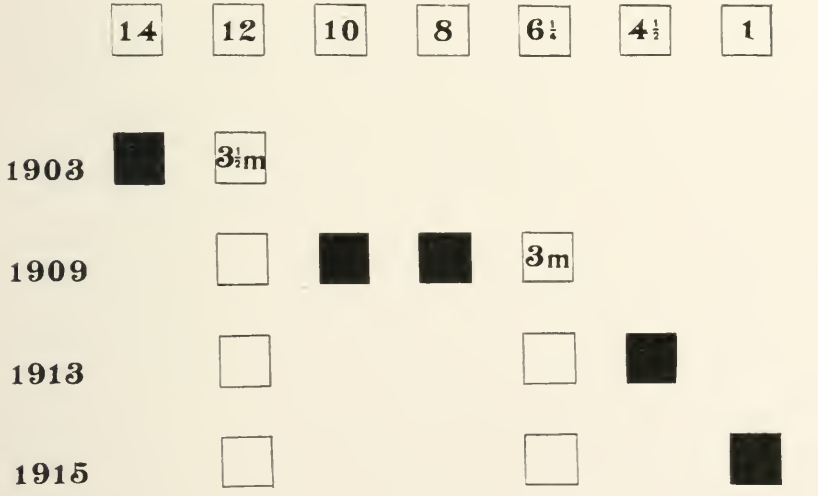

Chart 2.—A family of seven children. Illustrating the fact that infants who are *intimately* exposed to measles infection between the ages of 3 and 5 months and do not contract the disease, are frequently not infected when exposed to the disease in later life.

frequently are not infected when exposed to the disease in later life. Such contact must be intimate. In well-to-do families in which the infant has a separate nurse this may not occur. The accidental inoculation must take place after the third month, because before that time immunity being absolute there is no reaction and no immunity is con-

ferred. I have records of a number of cases, but the family illustrated on Chart 2 is the most striking. There were seven children aged 14, 12, 10, 8, 6¼ and 4½ years, and the youngest 10 months. The oldest child had measles in 1903; the second child was 3½ months old at the time and did not contract the disease. The third and fourth child had measles in 1909; the second, though exposed, did not contract it; neither did the fifth child, who was then 3 months of age. The sixth child had measles in 1913, and again the second and fifth were not infected. The seventh and youngest child had measles in 1915, and again the second and the fifth remained free.

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DISCUSSION

DR. LA FÉTRA: With regard to Dr. Herrman's first chart, I have been wondering why, in place of "diphtheria," he did not substitute "pertussis," because it seems to me that the chart would be more instructive if he had included whooping cough.

DR. KOPLIK: Some time ago, Dr. Baker of the board of health said that children with slight cough should be isolated at once when there had been measles in the family. At the very outset, sometimes five days before the eruption, there is a febrile movement, and with it the first appearance of the Koplik phenomenon. You get absolutely no reaction except a rising fever—100, 100.5, 101, and so on, until the eruption comes out; but during all this time there is seen the Koplik spots in the mouth. In my hospital service we isolate these children, and then wait patiently until the eruption comes out.

DR. HAMILL: I should like to ask Dr. Herrman whether he intended to imply that it is a good thing to expose children under 5 months to measles?

DR. HOLT: I wish to place on record another case of measles in a young infant. During the past winter I saw a typical case in an infant 7 weeks old. The disease was contracted from the mother, who was nursing the child.

DR. HERRMAN: I do not believe that there is any question that one could not be absolutely sure that a baby under 5 months could not contract the disease, but it is rare. I would not put myself on record as favoring the exposure of any child to a contagious disease, but experience shows that when these babies are exposed and contract the disease, it is of a very mild character. I suppose you would find in medical literature an occasional exception to that rule, but in the vast majority of cases it is true. I am trying out a method of immunizing them permanently, which is based on this relative immunity.

THE BACTERIOLOGY OF THE URINE IN HEALTHY CHILDREN AND THOSE SUFFERING FROM EXTRA-URINARY INFECTIONS *

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CHICAGO

The problem of pyelocystitis in infancy and childhood has become more and more important as our knowledge of the frequency of the infection has increased, and the possible serious consequences that it may entail. A few facts regarding pyelocystitis have been pretty well established, namely, that the infection is very much more common in girls than in boys, that the infecting organism is most frequently the *Bacillus coli,* and that the symptomatology of the condition is so indefinite as to make a diagnosis practically entirely dependent on the examination of the urine.

Regarding the mode of infection there seems to be considerable difference of opinion. In practically all articles on the subject, three possible modes of infection are given, namely, (1) ascending infection in the lumen of the urethra; (2) infections by way of the anastomosing lymphatics of large intestines and urinary tract; (3) infection by way of blood stream.

Regarding the third type of infection, the pathologic anatomy of the kidney proves that this type of infection does occur. In like manner the lymphatic route is quite definitely proved. The consensus of opinion in pediatric literature appears to be, however, that the infection by way of the lumen of the urethra is the commonest. The main facts in favor of the urethral route are the predominance of cases in girls, the shortness of the urethra, and the fact that the orifice of the urethra is constantly contaminated with colon bacilli.

Although it may appear that these three facts speak in favor of an ascending infection by way of the lumen of the urethra, nevertheless the question is far from being definitely settled.

In order to get a basis for future work it seemed essential first of all to determine the bacteriology of the normal urine and urethra. It

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is the object of this paper to record the bacteriologic findings of catheterized specimens of urine taken from thirty girl infants and from thirty-one girls over 2 years of age.

In an examination of the literature on urinary findings in health practically only a single paper, by Ross,[1] has been found. Ross catheterized nineteen normal children (age not given); of these nineteen specimens, eleven were sterile and eight showed a staphylococcus; of the eight, only three showed staphylococci in the second portion of the urine. Besides these, he catheterized eighty-seven girls, the specimens from none of whom were sterile. These contained in forty-three instances pure cultures of colon bacilli, in nineteen the *Bacillus proteus*, and in twenty-five instances a staphylococcus. It was impossible for us to tell from the text how these cases are to be classified, as only three of the colon group did he classify as evident pyelitis and only one in the proteus group. Of the staphylococcus he says, "there is no reason to attach importance to their presence." There are several criticisms to be made of this paper: first, that the urine was incubated for twenty-four hours in liquid mediums and then plated, and second, that the plates were incubated for only forty-eight to seventy-two hours. Under the first point it can be said that one type of organism may easily overgrow other organisms present so as to appear to be present in pure culture, and by the second method of treatment one gets no idea whatsoever as to how many organisms per cubic centimeter there are present in the urine, and it can also be said that many specimens will be sterile at the end of forty-eight to seventy-two hours and yet show a number of colonies at the end of a week.

The technic we employed in obtaining the specimens was as follows: The patient was placed on a table with the limbs widely spread apart, so that the orifice of the urethra was plainly visible. A sterile cotton applicator was now used to thoroughly cleanse the vagina, the external genitalia not being cleansed, while an assistant kept a constant fine stream of 1 per cent. lysol solution playing on the part. The region about the urethral orifice was naturally given special attention. Then with a dry sterile applicator the orifice of the urethra was mopped dry. A sterile catheter was now carefully introduced without touching anything but the orifice. In the infant there is usually a small fold of mucous membrane lying over and covering the urethral orifice, which

1. Ross: Bacteriology of the Urinary Tract in Children, Lancet, London, 1915, i, 484.

unquestionably protects the urethra from gross fecal contamination, but makes it almost impossible to avoid touching when introducing the catheter. If by any chance a portion of the vagina other than the orifice was touched a fresh catheter was taken. The urinary samples were collected in two or three sterile tubes, the flow of urine being controlled by compressing a piece of rubber tubing about 2 inches long that was attached to the glass catheter. These samples were labeled 1, 2, and 3, and were cultured separately so as to determine the difference between the first and last urine passed.

One cubic centimeter of urine was used in making the litmus-lactose-agar plates and blood-agar plates, 2 c.c. of urine in the deep dextrose-agar and deep blood-agar tubes. This variety of medium makes identification of the colon group easy, shows the organisms growing only on blood medium, and the deep tubes give opportunity for anaerobic growth. In the course of a few experiments Tubes 2 and 3 were found to be practically identical, so that in the majority of the cultures taken only 1 and 2 were used. Tube 1 was grown in deep dextrose-agar tubes and on a litmus-lactose plate. Tube 2 was grown on a litmus-lactose plate, a blood-agar plate, and in a deep blood-agar tube. In the passage of the catheter through the urethra a certain number of bacteria are carried into the bladder and are washed into the first portion of the urine; so that Specimen 1 represents urethral as well as bladder flora. In order to compare the first and last portion of the urine we have charted the cases as follows, designating the first portion as No. 1 and the last as No. 2.

The analysis of Table 2 shows the following:

The chemical and microscopic examination of the urine of the normal cases showed in no instances albumin, the specimens were all acid, a few of them cloudy with urates and phosphates. In a single instance there were a few leukocytes found, in three instances epithelial cells, and in no instance any casts.

Of the twelve normal cases five had sterile urine; of the remaining seven, two had organisms in the first portion of the urine, but none in the second. In one instance No. 1 was sterile when No. 2 contained 2 bacteria per cubic centimeter. In only one instance was a colon-like organism found in this entire series. A single colony of the *Bacillus alkaligenes* developed from 1 c.c. of the first portion of urine in Case 3. Of the remaining five specimens of No. 1 that were not sterile, three showed 1 organism per cubic centimeter and two, 3 organisms per

cubic centimeter. No. 2 contained 1 organism per cubic centimeter four times and 2 organisms once. In every instance in which more than 1 organism per cubic centimeter was found there were two types of organism identified.

The examination of the urine of the patients with extra-urinary infections showed very frequently pathologic constituents. The urine was alkaline three times, acid fifteen times. Albumin was present three times. On microscopic examination casts were present three times, a few leukocytes nine times, many leukocytes two times, and red blood corpuscles twice. The two specimens in which many leukocytes and red cells were found contained also a large number of casts, in fact formed a sediment that filled the bottom of the tube for about one-half inch. A diagnosis of pyelocystitis was made from the microscopic examination of the urine, but cultures did not bear out this finding. The infants were both very acutely ill, and the urine was highly concentrated. This finding emphasized the necessity of care in making a diagnosis of pyelocystitis from a single specimen, even when it is obtained by catheterization.

In Table 3, eighteen cases of extra-urinary infections, there were five instances in which the specimens were sterile. Of the remaining thirteen cases No. 1 was sterile once; in two instances there were 1 or 2 bacteria per cubic centimeter, in two instances from 3 to 5 per cubic centimeter, in two instances from 6 to 10 per cubic centimeter, in four instances from 11 to 20 per cubic centimeter, and in three instances from 21 to 50 per cubic centimeter. In like manner in No. 2 in five instances there was 1 bacterium per cubic centimeter, and in five instances there were from 2 to 5 per cubic centimeter, in one instance 7 per cubic centimeter, and in one instance 13 per cubic centimeter.

An analysis of the six cases in which colonlike organisms were found is shown in Table 1.

In their relation to the problem of cystitis this group of cases is perhaps the most interesting. Of eighteen cases, six showed the presence of gram-negative bacilli in the first specimens and in one-half of these in the second specimen also. In the second specimen in two instances there was a single organism per cubic centimeter, and in the third, 2 organisms. In each instance the flora of the second represents a dilution of the first, and in all probability represents urethral organisms.

The urines that showed gram-negative bacilli in both No. 1 and

No. 2 were from (1) a case of severe atrophy with marked retention of urine, 75 c.c. being obtained on catheterization, the catheter being passed while urine was flowing, No. 1 showing *B. coli* and gram-positive staphylococcus, and No. 2 showing a single colony of *B. coli;* (2) a case of bronchitis which had in Nos. 1 and 2 *B. enteritidis* and a gram-positive staphylococcus; (3) a case of pneumonia which had in No. 1 and No. 2 a gram-positive staphylococcus and *B. coli.*

Cases 4 and 5 of this series are especially interesting because the catheterized urine in both instances was loaded with pus cells and casts and gave a positive test for albumin, and yet No. 2 in one instance contained only 13 gram-positive staphylococci per cubic centimeter and the other 2 staphylococci and 2 colon bacilli per cubic centimeter.

TABLE 1.—ANALYSIS OF CASES IN TABLE 3 SHOWING COLONLIKE BACILLI

Case Number	No. 1		No. 2	
	Organisms per C.c.	Gram-Negative Bacilli per C.c.	Organisms per C.c.	Gram-Negative Bacilli per C.c.
13	20	10	1	1
15	6	3	4	2
19	20	10	4	0
24	30+	3	13	0
27	4	2	2	1
29	20	15	4	0

The first of those catheterized at a later date gave a sterile urine, no treatment having been instituted in the meantime. When one considers that in cases of cystitis the urine diluted 1 to 100 million or even 1 to 1 billion usually shows innumerable colonies, the importance of the finding of a single organism per cubic centimeter of undiluted urine is not to be overestimated.

To pass on to the analysis of Tables 3 and 4, it is seen that the normal patients over 2 years of age resemble those below 2 very much in the absence of finding on microscopic and chemical examination. In four cases there were a few leukocytes present and in one instance a positive test for albumin.

In the cases of extra-urinary infections there were only three that showed a positive test for albumin, five with small numbers of leuko-

TABLE 2.—Urinary Findings in Normal—

Case	Age, Mo.	Diagnosis	Examination of Urine					
			Reaction	Turbidity	Albumin	Cells	Casts	Bacteria
1	12	Normal	Acid	0	0	Few	0	0
2	7	Normal	Acid	0	0	Few	0	0
3	24	Normal	Acid	Phosphates	0	0	0	0
4	5	Normal	Acid	0	0	Few	0	0
5	11	Normal	Acid	Urates and phosphates	0	Epithelial cells; few leukocytes	0	0
6	9	Normal	Acid	0	0	0	0	0
7	8	Normal	Acid	0	0	Few	0	0
8	14	Normal	Acid	+	0	0	0	0
9	6	Normal	Acid	Amorphous yellow precipitate	0	0	0	0
10	14	Normal	Acid	0	0	0	0	0
11	12	Normal	Acid	+	0	0	0	0
12	13	Normal	Acid	0	0	0	0	0

TABLE 3.—Urinary Findings in Cases of Extra-Urinary—

Case	Age, Mo.	Diagnosis	Examination of Urine					
			Reaction	Turbidity	Albumin	Cells	Casts	Bacteria
13	8	Atrophy	Acid	Slight	Trace	0	+	0
14	12	Acute rhinitis	Acid	0	0	Few pus cells	0	0
15	14	Bronchitis	Acid	0	0	0	0	0
16	9	Bronchopneumonia	Acid	0	0	Few pus and epithelial cells	0	0
17	6	Exudative diathesis	Acid	+	0	Pus and epithelial cells	0	0
18	4	Exudative diathesis	Alkaline	0	0	0	0	0
19	8	Exudative diathesis	Acid	0	0	Few mononuclears	0	0
20	12	Exudative diathesis; tetany	Acid	0	0	0	0	0
21	13	Healing gland of neck	Acid	0	0	0	0	0
22	15	Healing gland of neck	Acid	0	0	0	0	0
23	10	Healing gland of neck	Alkaline	0	0	+	Few granular	0
24	11	Nephritis	Acid	+	+	Many R.B.C.; few W.B.C.	0	0
25	11	Nephritis	Acid	0	0	Few pus cells	0	0
26	18	Pneumonia	Alkaline	0	0	Few mononuclears	0	0
27	10	Pneumonia	Acid	++	+	R.B.C. +; pus ++	+	0
28	9	Rhinitis	Acid	Slight	0	Few round and epithelial cells	0	0
29	6	Tetany	Acid	0	0	0	0	0
30	6	Whooping cough	Alkaline	0	0	Few	0	0

—Cases of Patients Under Two Years of Age

Culture No. 1			Culture No. 2		
Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism	Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism
1	0	Gram-positive coccus	1	0	Gram-positive coccus
0	0	0	2	0	Gram-positive coccus; pseudo-diphtheroid
1	1	Bacillus alkaligenes	1	0	Gram-positive coccus
3	0	Hay bacillus; gram-negative bacillus in chains	1	0	Hay bacillus
3	0	Gram-positive coccus; pseudo-diphtheroid	1	0	Gram-positive diplococcus bacillus
1	0	Gram-positive coccus	0	0	0
1	0	Gram-positive coccus	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0

—Infections in Patients Under Two Years of Age

Culture No. 1			Culture No. 2		
Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism	Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism
22	10	B. coli communis; gram-positive coccus	1	1	B. coli communis
0	0	0	0	0	0
6	3	Gram-positive coccus; B. enterid.	4	2	Gram-pos. coccus; B. enterid.
5	0	Gram-positive coccus	4	0	Gram-positive coccus
22	0	Gram-positive coccus; pseudo-diphtheroid	7	0	Gram-positive coccus; pseudo-diphtheroid
0	0	0	*		
20	10	Gram-positive coccus; gram-negative bacillus	4	0	Gram-positive coccus
0	0	0	0	0	0
12	0	Gram-positive coccus; gas-forming anaerobe	1	0	Gram-positive coccus
6	0	Gram-positive coccus	1	0	Hay bacillus
0	0	0	1	0	Pseudodiphtheroid
50+	3	Gram-positive coccus; pseudo-diphtheroid; gram — bacillus	13	0	Gram-positive coccus
0	0	0	0	0	0
1	0	Gram-positive coccus	*		
4	2	Gram-positive coccus; B. coli communis	2	1	Gram-positive coccus; B. coli communis
2	0	Gram-positive coccus; gram-negative bacillus (anaerobe)	1	0	Gram-positive coccus
20	15	B. coli; gram-positive coccus; hay bacillus	4	0	Gram-positive coccus
0	0	0	0	0	0

* For Nos. 18 and 26 only one sample was obtained.

TABLE 4.—Urinary Findings in—

Case	Age, Yr.	Diagnosis	Examination of Urine				
			Reaction	Albumin	Cells	Casts	Bacteria
1	4	Normal	Acid	0	0	0	0
2	4	Normal	Acid	0	0	0	0
3	5	Normal	Acid	0	0	0	0
4	3	Normal	Neutral	0	0	0	0
5	5	Normal	Acid	0	0	0	0
6	6	Normal	Acid	0	0	0	0
7	5	Normal	Acid	0	Few mononuclears	0	0
8	5	Normal	Acid	+	0	0	0
9	5	Normal	Acid	0	Few round cells	0	0
10	5	Normal	Acid	0	0	0	0
11	5	Normal	Acid	0	Few pus cells	0	0
12	6	Normal	Acid	0	0	0	0
13	3	Normal	Acid	0	0	0	0
14	3	Normal	Acid	0	0	0	0
15	3	Normal	Acid	0	0	0	0
16	3	Normal	Acid	0	0	0	0
17	5	Normal	Acid	0	Few mononuclears	0	0
18	3	Normal	Acid	0	0	0	0

TABLE 5.—Urinary Findings in Cases of Extra-Urinary—

Case	Age, Yr.	Diagnosis	Temperature	Examination of Urine				
				Reaction	Albumin	Cells	Casts	Bacteria
1	10	Chorea	0	Acid	0	Few	0	0
2	11	Chorea	0	Acid	0	One group	1 granular and 1 waxy	0
3	10	Chorea	0	Acid	0	+ mononuclear and polymorph.	0	0
4	3	Tetany	0	Acid	0	0	Few casts and cylinders	0
5	3	Pneumonia	0	Acid	0	Few	0	0
6	12	Pneumonia	102	Acid	+	Few	+	0
7	11	Chorea	0	Acid	0	Few squamous	0	0
8	10	Endocarditis	97	Acid	Trace	Few	Hyaline and waxy	0
9	6	Meningitis; bronchitis	100	Acid	0	0	Few hyaline and cylindrical	0
10	3	Suspected cystitis	*	Acid	0	0	0	0
11	9	No diagnosis	103	Acid	0	0	0	0
12	6	Rhinitis	102	Acid	0	Pus cells	0	0
13	6	Suspected cystitis	0	Acid	0	0	0	0

* Fever for two weeks at a previous time.

—Normal Girls Over Two Years of Age

Culture No. 1			Culture No. 2		
Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism	Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism
0	0	0	0	0	0
0	0	0	4	0	Pseudodiphtheroid
0	0	0	0	0	0
0	0	0	21	0	Streptococcus (long chain)
1	0	Gram-positive coccus (short chained)	0	0	0
2	0	Gram-positive diplococcus	2	0	Gram-positive diplococcus
1	0	Gram-positive coccus; hay bacillus	0	0	0
1	0	Gram-positive coccus	0	0	0
0	0	0	1	0	Gram-positive coccus
0	0	0	0	0	0
5	0	Pseudodiphtheroid; 1 gram-positive coccus; 1 mold	0	0	Pseudodiphtheroid; mold
0	0	0	0	0	0
0	0	0	2	0	1 mold; 1 short-chained coccus
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
1	0	Gram-positive coccus	0	0	0

—Infections in Patients Over Two Years Old

Culture No. 1			Culture No. 2		
Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism	Number Organisms per C.c.	Number Gram-Negative Bacteria per C.c.	Types of Organism
1	0	Gram-positive coccus	2	0	Gram-positive coccus
3	0	Gram-positive coccus	2	1	Gram-positive coccus; B. proteus vulgaris
0	0	0	0	0	0
0	0	0	1	1	B. proteus vulgaris
4	0	Gram-positive coccus			
1	0	Gram ± staphylococcus			
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
1	0	Gram-positive coccus	0	0	0
0	0	0	0	0	0
1	0	Hay bacillus	0	0	0
1	0	Gram-positive coccus	0	0	0

cytes, one with numerous leukocytes (present in uncentrifuged specimen) and in four instances hyaline casts.

Of the specimens taken from girls above 2 years we find that the number of times sterile urine was obtained in both No. 1 and No. 2 was almost the same as in series 1. In thirteen cases out of thirty-one all cultures remained sterile. The number of bacteria per cubic centimeter in the different urines that showed organisms was very much smaller, however; in only one specimen were there more than five organisms per cubic centimeter. This urine contained twenty-one organisms per cubic centimeter of a long-chained, nonhemolytic streptococcus in pure culture. In only two instances was a gram-negative bacillus found, in both instances the bacillus proteus. In two instances a single colony of the hay bacillus was found. All the remainder were either gram-positive cocci or diphtheroid bacilli. Of the eighteen cases that showed growth in No. 1 or No. 2, in four No. 1 showed no growth; in nine No. 1 showed 1 organism per cubic centimeter; in five No. 1 showed from 2 to 5 organisms per cubic centimeter.

In the eighteen cases No. 2 showed in seven cases no growth; in three cases 1 organism per cubic centimeter; in four cases 2 organisms per cubic centimeter; in one case 4 organisms per cubic centimeter; in one case 21 organisms per cubic centimeter (blood plate).

In this group of thirty-one cases there are only two specimens of urine that contained gram-negative bacilli. These two cases were both in the first group of cases catheterized. The only case in which there were more than 5 organisms per cubic centimeter was a case in which twenty-one colonies of streptococci grew out of the blood-agar plate. There was no growth on the litmus-lactose plates. The small number of organisms probably all represent bacteria washed in from the urethra. This series of cases consisted of thirteen hospital cases, two acutely ill, the remaining suffering from chronic infections, and eighteen normal children in an orphan asylum.

SUMMARY

In 118 specimens of carefully catheterized urine from sixty-one different girls, sixty-one were sterile and fifty-seven contained bacteria. Of those from normal infants, thirteen were sterile and eleven contained bacteria. Of those from extra-urinary infections in patients under 2 years of age, none were sterile and twenty-four contained organisms. In those from girls over 2 years, thirty-eight were sterile

and twenty-two contained bacteria. The number of bacteria found in Series 1 was considerably larger than in Series 2. This may be explained by the fact that in the older children one can cleanse the urethral orifice much easier than in the infant and introduce the catheter directly into the urethra. The bacterial flora was practically the same in both series, gram-positive cocci and diphtheroid organism predominating, the former being present in practically every case in which any organisms were found. In no instance were gram-negative bacilli found in such numbers in both specimens that it seemed probable that it was more than an accidental contamination from the urethra.

CONCLUSIONS

1. Organisms of the colon bacillus group are not normal inhabitants of the female urethra.

2. In extra-urinary infections occurring in the first two years of life the colon group of bacilli are frequently found in the urethra (one-third of the cases).

3. In girls over 2 years of age the urine is almost free of organism, and in our series entirely free from bacilli of the colon group (eighteen normal, twelve other infections).

MENINGITIS IN THE NEW-BORN AND IN INFANTS UNDER THREE MONTHS OF AGE*

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Meningitis in the new-born is not only poorly described in the literature, but a careful perusal of the cases thus far published must lead to the impression that the condition is overlooked, or, at first, scarcely suspected. The reason for this is at first glance evident. The new-born does not react to infection in a way to draw the attention. There may be rational symptoms of almost any condition which will inevitably remain unrecognized unless carefully looked for. The nervous and physical reaction to irritation in the new-born is extremely slow and obscure. It takes some time for a clinical picture to develop, and then when fully developed the complex is apt to remain uncertain. Primary meningitis in the new-born is not as common as the secondary infection, following general septic infection of the new-born. There are certain objective signs of meningitis which are unmistakable, and yet other signs occurring in infants at a more advanced age must be necessarily absent, as they are very difficult of interpretation in the new-born. Many writers give the impression that meningitis in the new-born is mostly secondary to other diseases, such as otitis, syphilis or sepsis. This is not so. Many cases escape recognition because the onset is insidious, and it is only after the symptoms have developed to the extent of giving the picture of cerebral pressure that the case is suspected to be one of meningitis. In some states of extreme exhaustion, or atrophy, meningitis is revealed at necropsy only. I have collected all the cases from my hospital service, and with these include a consideration of some cases observed outside of the hospital. The new-born reacts very slowly to cerebral irritation, and the picture of meningitis is at first masked by rational symptoms which are apt to mislead. This is very evident after a severe labor, when the infant is born with all the signs of having passed through a critical period. In most cases there is a caput succedaneum, and in many cases of intensive delivery with forceps there are wounds about the head and neck, which neces-

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sarily make the infant for the time being limp, and reactionless. It takes at least from twenty-four to forty-eight hours for the local traumatisms about the head to subside, and then if any rational symptoms present themselves they must be carefully analyzed. In some cases a cerebral suggillation may closely resemble in its symptoms a meningitis. A temperature, even accompanied by convulsions, may mean a simple evanescent sepsis. In the new-born even with cerebral symptoms the body remains limp; we do not have the active development of rigidity of the neck, Brudzinski and Kernig signs seen at a later period of infancy. In drawing the picture of meningitis of the new-born, we can only select the cases observed from the onset and interpret the symptoms for future guidance. Cases which come to the hospital, as will be seen from a reference to my series, do so when the disease has been certainly present for weeks, and only when fully developed, as a result of accumulation of fluid in the ventricles of the brain, has the mother or guardian noted any symptoms. In this respect we must not interpret the histories literally. When a mother states her infant was taken at six weeks with convulsions, fever, and unconsciousness, the presumption is that the condition producing these symptoms may, from what we know of the process, have been existent much longer than the history states. I therefore consider that an infant six weeks of age, coming to the hospital with bulging fontanel, occasional or frequent convulsions, fever, or even normal temperature, with a purulent fluid obtained by lumbar puncture, must have been ill for weeks; the symptoms have been misinterpreted or so insidious as to have rationally been overlooked, until the stage of accumulation of fluid and cerebral pressure revealed the affection.

The symptom most characteristic of meningitis in the new-born is first of all, convulsions. These convulsions may be frequent; at first one or two convulsions occur and with them a high temperature. The temperature at first may be quite high—105 in one of my cases. In most cases the convulsions are repeated at first, and if they recur, do so at odd intervals. This recurrence of convulsions in the new-born is quite characteristic. They recur from two to four days after birth, and the temperature may not run so high a curve as at first. On the contrary, the temperature may drop gradually and after the first week only range a degree or two above the normal, and finally fall and run 100 in the rectum, while the disease is still in progress. A very characteristic feature of meningitis is the restlessness of the infant.

After the initial convulsion the infant will have periods of constant crying and restlessness with normal conditions of the bowel. The conditions about the head and fontanel are at first misleading. The fontanel may show bulging only days or weeks after the onset, so that at first the fontanel gives no clue. It may show normal conditions. Before fluid accumulates, we get no Macewen, which is characteristic, for after birth, even normal infants show an increase of fluid, as compared to later infancy, so that the percussion of the skull is extremely difficult of interpretation. Kernig's sign is, as a rule, absent and the new-born lies even in the normal state with knees drawn up, and, in cases of undoubted meningitis, the Kernig is not elicited, nor is the Brudzinski sign, until a much later period, as can be seen by reference to my histories. The new-born lies, as to the head and neck, even in the normal state, quite limp, and in meningitis the rigidity of the neck is elicited at first rarely, or not at all, until weeks post partum. A very characteristic history of primary meningitis ab initio in the new-born is the following: A male infant, 2½ weeks old, was delivered normally without forceps. Three days after birth the patient, apparently well at birth, developed convulsions with a temperature of 101. These convulsions were repeated and then ceased; after an interval of two days they returned, but now in the form of tremors or twitchings of the extremities of the muscles of the face. On the eighth day the infant again had outspoken convulsions, and in one of them went into collapse. The infant during this time had a varying temperature, and after two weeks the temperature subsided. It was then noticed that the fontanel was bulging, the sutures of the skull could be distinctly outlined and the infant did not notice the light; the pupils did not react. It will be seen in this case that not until the fontanel was bulging did any thought enter the mind of the physician that a meningitic process might be present. I wish to emphasize the fact that after the initial convulsions, in the interval between the general convulsions, a very characteristic twitching of the face occurred at intervals and this at times was accompanied by twitchings of the muscles of the extremities.

Very characteristic of purulent cases are convulsions accompanied by a fall in the temperature and symptoms of collapse, with cyanosis resembling chills. This I have observed in a case of coli meningitis in the new-born, in which there was a pyelitis, which was the primary infection, and from which the meningitis resulted as a secondary infec-

tion. This infant on the thirteenth day of life had chills, preceded by convulsions, which ushered in the meningitis. Another very characteristic symptom is constant vomiting; the vomiting is more in the form of a regurgitation, and has no relation at all to the time of feeding. In some cases, as in a new-born child seen at one of the maternity hospitals, in which a pneumococcus meningitis was established by necropsy, there were no convulsions, but only twitchings of the extremities, apathy, and, on the tenth day, chills, cyanosis and bulging fontanel, with apathy, no rigidity or Kernig or Brudzinski. A peculiar groaning is very characteristic. The infant in breathing emits a groaning noise, as if pressure were exerted on the cerebrum similar to what is observed in brain compression in the adult, due to any cause. The temperature may at first be quite high, but after marked remissions, or even intermissions, the temperature may after a week drop to the normal and stay there, or it may run a degree or less above the normal, but rarely mounts very high. This is not generally known. The condition of the fontanel, as stated elsewhere, at first may be absolutely normal, in fact, I have compared the fontanel in one case with that of a normal new-born infant and found no difference in the early days of a meningitis. It is only when fluid accumulates rapidly or later in the disease that the fontanel becomes prominent. What are, then, the objective symptoms which would lead us to suspect a meningitis in the newborn? The first are convulsions, repeated with convulsive movements of the eyes and muscles of the extremities in the intervals, fever, constant restlessness, with vomiting; with this a suppressed groaning respiration and a temperature curve, at first very high, then gradually remitting or intermitting, and, finally, falling to or near the normal. Most of the cases after a week's duration develop a rigidity of the neck and a drawing back of the head, which indicates clearly the nature of the affection. In other words, opisthotonos is slow in developing. The most frequent diagnosis apt to be ventured in a meningitis is tetany. Tetany in the new born is an even rarer occurrence than meningitis, and to make the diagnosis of tetany in the new-born is to overlook the more probable condition of meningitis. Meningeal hemorrhage, as a result of pressure during the delivery, gives a syndrome closely resembling meningitis, but in this condition there is no fever and there are other symptoms, such as cyanosis, irregular respiration, or even apnea, which would not be present in meningitis in the early stages. The con-

vulsions in meningeal hemorrhage are not repeated, as a rule, and the fontanel has a board-like feel, lacking pulsation, and does not become prominent as the disease progresses. A suspicion of meningitis, in the face of equivocal symptoms, would indicate lumbar puncture.

The Nature of Infection.—Of twelve cases, of which I have an actual examination bacteriologically of the fluid obtained by lumbar puncture, four contained streptococcus in pure culture, three pneumococcus, four meningococcus, and one colon bacillus, the last as a result of systemic infection from a colon pyelitis. The real pathogenesis of all cases of meningitis in the new-born, whether the meningitis occurs as a primary manifestation or as secondary, or with foci of infection, such as in some of my cases, arthritis or pyelitis must be considered in the nature of an infection of a septic character. In one case of meningococcus infection there was a negative blood culture. In one streptococcus case accompanied by arthritis, the blood culture was positive, revealing streptococci. The fluid obtained by lumbar puncture is, as a rule, purulent if there is a streptococcus or a pneumococcus meningitis. In meningococcus cases it may simply be cloudy or colorless. It may be so thick and viscid in all forms as to flow with difficulty from the needle. The cytology is a polynuclear one and the leukocytes may make up 100 per cent. of the cells. The albumin in the puncture fluid of the cases here attached seems to vary from 4 mm. to 8 mm. It may be of interest to note that in the meningococcus cases in which ventricular puncture was made meningococci were found in the ventricular as well as in the lumbar fluid.

The prognosis of meningitis in the new-born is, as may be a priori surmised, very grave. All the streptococcus patients died, as well as the pneumococcus patients. The colon patient developed hydrocephalus, and died later in infancy, whereas all but one of the meningococcus patients died. The only one which recovered did so with hydrocephalus. It is noteworthy that the prognosis is so grave and still I think that the meningococcus cases, if discovered early, may be brought to a quiescent period by prompt treatment. The only danger is that the subsequent hydrocephalus may not limit itself, but may increase to such an extent as to cause idiocy. Lumbar puncture, I find, is most apt to meet insurmountable obstacles in the new-born, where the cerebral canals leading into the subdural space are exceedingly narrow in caliber, and at the third or fourth puncture the fluid is apt not to flow from the subarachnoid space. This occurred in a case

of meningococcus meningitis, which made a recovery. In this case, after the third introduction of serum, the canal of Majendie closed, thus making further therapy impossible, except through the route of ventricular puncture. This patient was punctured on the tenth day of life. In two cases in my hospital service, one a meningococcus, another a streptococcus case, ventricular puncture was performed. In both the procedure was of no avail, though in one case the ventricles were irrigated with methyl-blue. From what I have seen of ventricular puncture—and my experience ranges over a number of cases, not only in the new-born, but at a later period of infancy — it is a very unsatisfactory procedure. The new-born seem to go into a condition of collapse after the ventricular puncture, from which they do not recover. The question naturally presents itself as to how in the cases not complicated by other symptoms of sepsis of the new-born, these infants contract a pneumococcus or meningococcus meningitis. In those cases which I have followed in maternity institutions I found that the infants were born after a stormy or prolonged labor; that methods of resuscitation had been rigorously applied, among others, mouth to mouth and catheter suction. The natural inference in these cases is that the infection took place possibly from the mouth of the accoucheur to that of the infant. Especially as in these cases there are recent wounds in the mucous membrane of the mouth, the contention of Epstein that systemic infections may take place through these buccal solutions of continuity seems not unlikely.

SUMMARY OF CASES

Year	Age	Diagnosis	No. Cases
1909	6 weeks	Sepsis neonatorum: arthritis; meningitis (streptococcus)	1
1910	7 weeks	Meningitis (streptococcus)	1
1912	New-born	Meningitis (colon bacillus) followed by hydrocephalus; died at 16 months	1
1913	10 weeks	Meningitis, cerebrospinal (meningococcus)	1
	8 weeks	Meningitis (pneumococcus), convulsions	1
	3 months	Meningitis (pneumococcus), congenital syphilis, Hochsinger thickening of skin	1
	6 weeks	Meningitis (streptococcus)	1
	3 months	Meningitis, cerebrospinal (meningococcus)	1
1914	6 weeks	Meningitis (meningococcus)	1
1915	3 months	Meningitis, cerebrospinal (streptococcus)	1
1915	New-born	Meningitis (pneumococcus) (Maternity Hospital)	1
1915	New-born	Meningitis (meningococcus) (Maternity Hospital): hydrocephalus	1
		Total number of cases	12

CASES FROM MT. SINAI HOSPITAL, CHILDREN'S SERVICES *

CASE 1.—Pauline, aged 6 weeks, was admitted June 16, 1909; died June 26, 1909. A diagnosis of sepsis neonatorum, arthritis, meningitis (streptococcus), was made. The past history showed a full term, normal labor; breast-fed. No previous illness. The present illness began three days before admission (?) with fever. Child cries when touched. Yesterday mother noticed redness and swelling of right hand and today of right foot. No vomiting. No convulsions. Bowels normal.

Examination: General condition good; well nourished. Anterior fontanel admits one finger. Slight convergent strabismus. Pupils equal, react to light. The tongue is clean. The skin is of a purplish hue on exposure to air. The lungs are negative. The heart is rapid and regular, but there are no murmurs. Epigastric pulsation is present. The pulses are equal, rapid, regular and of fair force. The liver is at the fourth or fifth space, felt one finger below ribs. The spleen can be felt just below the ribs. There is edema and swelling of right upper extremity, which pits on pressure. The extremity seems to be tender. The swelling is most marked in the hand and forearm. In the outer part of the palm of the hand is a red, tender area. There is no paralysis. Few enlarged glands in right axilla. There are redness, swelling and tenderness of the right foot at the metatarsal phalangeal joint, with slight edema of the dorsum of the foot.

June 17. Redness of right hand is more marked. Leukocytes, 20,600; polymorphonuclears, 56 per cent.; small lymphocytes, 40 per cent.; large lymphocytes, 4 per cent.

June 18. Left hand and forearm is swollen, tense, apparently tender, same region as other hand. All bones are tender to pressure.

June 18, 9 p. m. Edematous swelling of right forearm just above right wrist, probably involving epiphysis of radius and ulna. Edematous swelling of dorsum of left hand. Similar swelling over metatarsophalangeal joint of right big toe. No fluctuation in any. Advice, waiting. At first sign of fluctuation swelling to be incised. Wet dressings to be applied.

June 20. Incision and drainage of multiple abscesses. One abscess on back of left hand, one on palmar surface of right hand, leading up to one inch above ligament. One on each foot. Each was opened and drained. Wet dressings.

June 22. Left shoulder slightly enlarged, tender. Swelling and induration in front part of left shoulder. Slight icterus. Leukocytes, 12,400; polymorphonuclears, 45 per cent.; large lymphocytes, 8 per cent.; small lymphocytes, 47 per cent.

June 23. General condition worse. This afternoon had general clonic convulsion.

June 24. Child unconscious. In frequent tonic, occasional clonic convulsions. Head turned to right with conjugate deviation of eyes. Fontanel not bulging. Local condition: Moderate purulent discharge from all the foci. Lumbar puncture at level of crests—12 c.c. of cloudy fluid obtained.

June 25. General condition worse. Several convulsions during past twenty-four hours. Child unconscious.

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* The bacteriologic examinations were carried out by the bacteriological laboratory of the hospital.

Temperature ranged from 100 to 104.8.

Laboratory Examinations: June 18, blood culture: *Staphylococcus albus*. June 20, culture of pus: streptococcus. June 22, blood culture: *Staphylococcus albus* and streptococcus. June 24, cerebrospinal fluid: streptococcus.

Radiographic Report: June 26, no change in the bones of the right forearm, wrist and hand. There is present complete flexion of the finger.

CASE 2.—Morris; aged 7 weeks; admitted Dec. 30, 1909; died Jan. 1, 1910. A diagnosis was made of streptococcus meningitis. The previous history showed a normal delivery. There had been occasional regurgitation after taking the breast. The present illness began ten days before with convulsion. The child appeared ill, vomited two or three times a day, and developed fever. Began to have repeated convulsions and unconsciousness two days ago. Some rigidity of jaw.

Examination showed the child unconscious. General convulsions produced on attempt at examination. Neck not rigid. Fontanel bulging. Jaw rigid. Rigidity of extremities. Marked Kernig. Few râles posteriorly over lungs.

December 30. Lumbar puncture showed thick pus containing streptococcus. Ten c.c. antimeningococcus serum introduced.

Temperature ranged from 98 to 102.2.

CASE 3.—Irving; aged 10 weeks; was admitted Jan. 11, 1913; died Jan. 12, 1913. A diagnosis of cerebrospinal meningitis was made.

The family history showed that the mother's first baby died of meningitis at the age of 2 months. The past history was that of normal delivery, with no diseases of infancy.

The present illness began suddenly three days before with fever and irritability. No convulsions, no vomiting at onset. Yesterday baby vomited (curdled milk) and mother noticed that all motions of neck became painful. Today mother noticed mottled rash on body and extremities. Stools, three or four daily; greenish, no blood.

Examination showed the general condition fair, but the patient irritable. The child seemed well nourished. There was marked rigidity of neck. Anterior fontanel admitted two fingers, tense, bulging. Posterior fontanel admitted tip of one finger. The pupils equal, reacted to light, no palsies. There were no teeth, gums negative. Throat somewhat congested. A few posterior cervical glands were enlarged. Scattered over the entire chest and abdomen anteriorly and posteriorly, also over upper and lower extremities was a profuse crescentic, rose-colored, macular eruption, disappearing on pressure. No desquamation. This eruption was more confluent over the neck, where small areas of erythema were present, extending from ears to chin. Nothing was on face above the level of the ears. The chest expansion was good, the respirations regular. The lungs were negative. The heart action was rapid, regular, with good force. The pulses were equal and regular with good force. The liver was felt three fingers below. The spleen was not felt. The abdomen was distended, tympanitic, but there were no masses. The genitals were negative, the testes descended. The upper extremities were negative, the lower showed knee-jerks exaggerated; no Kernig, inconstant Babinski.

January 12, 2:30 a. m. At lumbar puncture 8 c.c. of very turbid fluid were obtained under very low pressure. About 10 c.c. of Flexner serum were injected, when child began to breathe very poorly, and then stopped breathing. In spite of artificial respiration for one-half hour, the child died.

The temperature ranged from 101.2 to 103.2.

Laboratory examination on January 12 of cerebrospinal fluid showed albumin, 8 mm.; bacteria, meningococcus; reduction, none; cytology, polymorphonuclears, 100 per cent.

CASE 4.—Lilly; aged 8 weeks; was admitted Feb. 7, 1913; died Feb. 8, 1913. A diagnosis of pneumococcus meningitis, with convulsions, was made. The family history was negative. The past history showed that the child was born at full term in normal labor; child blue at birth and was asphyxiated, necessitating artificial respiration. She was breast fed. From 1 week of age the child had had a rash on the body.

The present illness had an onset three days before, with cough, fever and diarrhea. The stools were green and watery. Yesterday the child had a convulsion. She has vomited several times since the onset.

Examination showed that the general condition was poor; she was fairly well nourished. The child moans more or less continuously. She lies with the head retracted and hands and feet in tetanic spasm. The anterior fontanel was open, admitting four fingers; it was tense and bulging. The posterior fontanel was open. There was slight rigidity of the neck. The eyelids were puffy, and there was slight discharge from both eyes. The ears and mastoids were negative externally. There was a slight mucoid discharge from the nose. The tongue was moist. Scattered over the back of the neck and in the folds of the skin at the axillae and groins, covering the vulva and the buttocks and extending on the abdomen and thighs was a scaling, erythematous, dry, seborrheic eruption. The skin itself felt hard, not raised. The scales were large, flat and extended down to the feet. There were excoriations around the vulva and anus, oozing serum. The lungs were negative. The borders of the heart were normal, there were no murmurs and the action was good. The pulses were equal, regular, and of fair force. The liver was felt two fingers below the ribs. The spleen was not felt. The abdomen large and tympanitic, but there were no masses. The extremities showed carpopedal spasm. Knee-jerks were obtained and a slight Kernig, with bilateral Babinski. There was a slight vaginal discharge.

The temperature ranged from 101 to 102.8.

Laboratory examination on February 13 of the cerebrospinal fluid showed polymorphonuclears, 100 per cent.; albumin, 6 mm.; reduction, none; bacteria, pneumococcus in spreads and culture.

CASE 5.—John; aged 3 months; was admitted Feb. 10, 1913; died Feb. 12, 1913. Diagnosis, pneumococcus meningitis, congenital syphilis, and Hochsinger thickening of the skin. The family history showed the mother had been pregnant seven times; there had been four stillbirths; one child had died in infancy; one child was alive and well. The past history showed that the patient was a full-term child, born in normal labor, and had been breast fed. The present illness had an onset six weeks before, with a rash over the entire body and snuffles. These symptoms disappeared under treatment. Yesterday morning the child began to snuffle again and had a slight cough. This morning he vomited and had a convulsion. There was no diarrhea, and no urinary disturbances.

Examination was made February 10: The general condition was poor. The patient was very irritable, moaning, and very pale. The anterior fontanel admitted three fingers, and was tense and bulging; the posterior admitted one finger, and was rather tense. There was marked rigidity of the neck. The pupils were equal, reacted to light, and there were no palsies. There were no

teeth, the gums were fair, the tongue moist. There were two small petechiae on the palate. The chest was symmetrical, with expansion fair. The lungs were negative. The heart action was rapid, regular, forcible, and there were no murmurs. The liver was felt three fingers below the ribs. The spleen was not palpable. The abdomen was lax and tympanitic. There was scaling of the palms and soles; there were no blebs. There was a maculopapular eruption of the extensor surfaces of legs and feet. The eruption was for the most part hemorrhagic. There was a copper-colored papular eruption around the anus. The extremities showed knee-jerks markedly increased. There was bowing of both tibiae, and a slight Kernig. Babinski was present when Kernig was obtained. Both testes were descended. The scrotum was large and covered with papules.

February 11 lumbar puncture was made, and 10 c.c. turbid fluid was removed.

The temperature ranged from 98 to 108.

Laboratory examination was made on February 12. The Wassermann reaction was positive. On February 13 the cerebrospinal fluid showed marked increase in globulin, with Wassermann reaction positive. The cytology showed polymorphonuclears, 100 per cent.; reduction, absent; albumin, 8 mm.; bacteria, pneumococcus in spreads and cultures.

CASE 6.—Henry; aged 6 weeks; was admitted May 27, 1913; died May 28, 1913. A diagnosis of streptococcus meningitis was made. The past history showed delivery at seven months. The present illness began about three days before; rather suddenly the child became feverish, had convulsions, which have been repeated at frequent intervals; he vomited at the onset. He refused nourishment. The bowels were constipated. At times there was a cough.

Examination showed the general condition to be poor; the child was restless and breathed with difficulty. The eyes showed no palsies. There was marked bulging of anterior fontanel, slight rigidity of the neck, and the tongue was slightly coated. Posteriorly there was dulness over the right base of the lungs, with diminished breathing; bronchophony was present. The heart action was regular, rapid, the sound of fair force, and there were no murmurs. The pulses were imperceptible. The abdomen was negative. Kernig was present, especially on right side, no Babinski or clonus. There was marked spasticity of all extremities.

May 27 lumbar puncture was made and 20 c.c. turbid fluid under marked pressure were removed. There were 15 c.c. of meningitis serum injected.

The temperature ranged from 102.4 to 103.

CASE 7.—David; aged 3 months; was admitted Sept. 15, 1913; died Sept. 22, 1913. Diagnosis of meningococcus cerebrospinal meningitis. The past history showed no previous illness; there had been normal birth, and the child had been breast fed. In the present illness the child had been sick for a week with green stools and slight cough for the last three days. Had been apathic, but there had been no convulsions. The neck had been stiff for the last two days.

Examination showed the general condition to be poor, child extremely irritable and restless, shrieking loudly. The pupils were equal, and reacted to light; there was internal strabismus of the left eye. There were no teeth. The tongue was clean. There was marked bulging of the anterior fontanel. The lungs were negative. The heart action was rapid and of fair force. The pulses were equal, regular and rapid. The liver and spleen could not be felt. The abdomen was lax, tympanitic, and showed marked tache cérébrale. The

knee-jerks were exaggerated. There was bilateral Kernig sign, Brudzinsky and Babinski.

September 16 lumbar puncture was attempted, but nothing was obtained. Ventricular puncture was made and 35 c.c. bloody fluid were obtained. Twenty-five c.c. Flexner serum were injected.

The temperature ranged from 101 to 105.4.

Laboratory examination made September 16 of the cerebrospinal fluid showed polymorphonuclears, 100 per cent.; bacteria spreads and cultures, meningococcus; albumin, 8 mm. ring; reduction, none.

CASE 8.—Louis; aged 6 weeks; was admitted Aug. 2, 1914; died Aug. 7, 1914. A diagnosis of meningococcus meningitis was made. The family history showed that there had been two other children, one of whom died of pertussis. The mother had two miscarriages. There was a past history of difficult labor, but not instrumental; the child had been breast fed up to the time of entrance and had had no previous illnesses. The present history showed that the day before at 5 a. m. the child began to cry and had fever (104.5) and became "stiff." At 4 p. m on the day of admission he had a convulsion lasting ten minutes; the convulsion was general. The bowels moved frequently, green stools, with catharsis.

Examination showed that the child cries much. The eyes were normal, the fontanel prominent when the child cried. There was no rigidity of the neck. The heart and lungs were negative. The abdomen was moderately distended. The extremities showed no paresis, and no abnormal reflexes.

August 3 lumbar puncture was performed and 2 c.c. of turbid, slightly blood-tinged fluid were obtained under increased pressure.

August 4 lumbar puncture was again done and 1 c.c. of turbid fluid was obtained under appreciable pressure. By ventricular puncture 10 c.c. of blood-tinged fluid were obtained under pressure. At this time 10 c.c. of antimeningococcic serum were given by lumbar puncture. At 4:30 p. m. the child went into a general clonic convulsion, which lasted for ten minutes. He was cyanosed and there was a regurgitation of fluid. The face, neck, arms and legs were twitching. The fingers were tightly clenched over the thumbs. There were slight Kernig and marked Brudzinski, with irritability on head flexion.

August 5 lumbar puncture disclosed the presence of a cloudy fluid and 2 c.c. were removed. Ventricular puncture at the left angle also gave cloudy cerebrospinal fluid, and 15 c.c. were removed. Through ventricular puncture antimeningococcus serum, 25 c.c. diluted with saline and methylene blue, were injected slowly. At the expiration of about twenty minutes blue cerebrospinal fluid flowed from the lumbar puncture needle, which was left in place. The condition was fair throughout, 2 grains of camphor being given to ward off any possible collapse. The pulse varied with the intraventricular pressure, slowing with increase of pressure. There was no change in respiration.

August 7 the convulsions continued. The fontanel was no longer bulging. The child had nystagmus and was spastic. The pulse was rapid but regular. Ventricular puncture was made and 5 c.c. of cloudy amber fluid were obtained under increased pressure, somewhat blood tinged. Five c.c. of antimeningococcic serum were introduced. On lumbar puncture 3 c.c. of cloudy, amber fluid were obtained under pressure, somewhat blood tinged. Ten c.c. of antimeningococcic serum were introduced.

The temperature ranged from 100 to 104.6, with a rise to 106 on the day of death.

Laboratory Examinations: On August 3 the cerebrospinal fluid showed 95 per cent. polymorphonuclears; reduction, none; bacteria, meningococcus; albumin, 4 mm.

August 4 the ventricular cerebrospinal fluid showed fresh blood present; bacteria, meningococci; albumin, 5 mm. ring; reduction, none. The cerebrospinal fluid showed 95 per cent. polymorphonuclear leukocytes; bacteria, meningococci; albumin (quantity insufficient); reduction (quantity insufficient).

August 5 spinal cerebrospinal fluid showed 95 per cent. polymorphonuclear leukocytes; bacteria, meningococci; albumin, 5 mm.; reduction, none. The ventricular cerebrospinal fluid showed 95 per cent. polymorphonuclear leukocytes; bacteria, meningococci; albumin, 4 mm.; reduction, none.

CASE 9.—Leonard; aged 3 months; was admitted Feb. 26, 1915; died March 1, 1916. Diagnosis, cerebrospinal meningitis (streptococcus). The past history showed a full-term child, high forceps delivery, breast fed, with normal development. The present illness began ten days before with slight fever and constipation, which continued off and on until the morning of the previous day, when the child suddenly became very drowsy and lay motionless for hours; this condition continued until the afternoon of admission, when the child had three general convulsions within five hours, each lasting from three to five minutes; there was frothing at the mouth but no vomiting. The bowels were kept open by catharsis; urination was normal.

Examination showed the general condition to be fair. The child was acutely ill, but he was well nourished. There was slight retraction of the head. Macewen's sign was marked. The anterior fontanel was three fingers wide, distinctly bulging and tense. There was double internal strabismus. The pupils were equal, regular and reacted to light. The lungs were negative. The heart action was rapid, regular, and of fairly good quality. The abdomen was rounded, soft and tympanitic. The Brudzinski sign was present, and there was slight Kernig on the right side. The skin showed taches and a small ulceration over the right scapula.

February 26, 9:15 p. m. The child had generalized convulsions lasting three minutes, affecting chiefly the left arm and foot, with head turned to the left. At 11 p. m. lumbar puncture was performed and 25 c.c. cloudy fluid was obtained under high pressure. Twelve c.c. serum were slowly introduced.

February 27, 9:30 a. m. Lumbar puncture was performed and 20 c.c. very turbid fluid were obtained under high pressure. From 12 to 15 c.c. serum were injected, passing in very slowly and with difficulty. Blood count showed leukocytes, 12,000; polymorphonuclears, 85 per cent.; lymphocytes, 15 per cent.

February 28 the child was semiconscious; the fontanel was bulging. Brudzinski sign was very marked. The general condition was very poor. Four c.c. thick purulent fluid under pressure were withdrawn by right ventricular puncture. Ten c.c. polyvalent antistreptococcic serum were injected.

March 1. The general condition was worse in the morning. There was double internal strabismus, fontanel bulging, respiration and pulse irregular, and twitching of both arms and legs. The child died.

The temperature ranged from 101.4 to 103.2, with rises to from 104.8 to 106.4 on the day of death.

Laboratory examination made February 26 of the cerebrospinal fluid showed polymorphonuclears, 95 per cent.; mononuclears, 5 per cent.; bacteriology, streptococcus; albumin, 6 mm. ring; reduction, none.

PRIVATE CASES

CASE 1.—A boy, new-born, was circumcised on the eighth day, and ran a fever from the time of circumcision to three days subsequent. An examination proved negative as to chest, heart, lungs and abdomen. The sensorium was free, and there were no signs of meningitis.

Examination of the urine showed *Bacillus coli* pyelitis. The baby ran an irregular temperature one week, when there was a chill, combined with repeated convulsions, and collapse. After these signs meningitis developed. The infant did not appear to see light. The fontanel became prominent. Lumbar puncture revealed a colon bacillus meningitis. Hydrocephalus developed and the infant died at 16 months of asthenia and necrosis of both eyes. Three lumbar punctures were made. The diagnosis was colon bacillus meningitis.

CASE 2.—A boy, new-born, was seen at the Maternity Hospital on the ninth day of the disease. He had been limp and reactionless from birth. There was no rise of temperature. The child when seen was limp and had a peculiar groaning respiration, Cheyne-Stokes in rhythm. The pulse was slow and irregular, the fontanel tense.

Examination showed no retraction of the head, but distinct fluid in the head, no bulging of fontanel, although tense. A few râles were perceptible at the bases of the lungs. A diagnosis of meningitis or hemorrhage was made. Lumbar puncture revealed pneumococcus in the puncture fluid.

Necropsy of the brain and cord showed a serofibrinous exudate over the surface of the brain and over the posterior surface of the cord. It was, therefore, a pneumococcus meningitis.

CASE 3.—A boy, new-born, was seen at one of the private hospitals of the first rank. He had been running a fever from birth. I saw the baby on the third day of his life. There had been a very prolonged labor, and birth after thirty-six hours. The infant was born in suspended animation, requiring vigorous efforts at resuscitation. When seen on the third day the child was in excellent condition.

Examination showed the head negative, the fontanel normal, and there were no marks of delivery. The urine showed blood, blood casts and albumin. The child had a temperature of 105. He had one convulsion, which was not repeated. The umbilical stump seemed normal. The patient ran a temperature of 105 or 103, irregular, remittent, and, finally, on the tenth day, the temperature became normal. During this time, however, the child developed slight twitchings about the muscles of the face, especially on the left side. He took his food regularly, but had periods of restlessness and crying, especially at night. He was artificially fed. On the ninth day it was noticed that there was slight retraction of the head, but not excessive. The fontanel was not bulging. In view of the continued twitching of the muscles, the preceding convulsion, and the temperature, a diagnosis of meningitis was made.

Lumbar puncture was performed and expert examination of the fluid showed meningococcus. Flexner serum was injected. Two subsequent punctures were made and serum introduced. At the fourth puncture no fluid was obtained.

A culture of the blood was made, but no microorganisms were found. The patient made an apparently good recovery. The drawing back of the head, which became marked, gradually disappeared. The infant is still alive, has a hydrocephalus, is exceedingly bright and holds the head up. The hydro-

cephalus, apparently, has come to a standstill. The child is now 9 months of age and has a head circumference of 51 cm. The disease was a meningococcus meningitis.

30 East Sixty-Second Street.

DISCUSSION

DR. TALBOT: I should like to ask Dr. Koplik how he differentiates the meningococcus from the gonococcus.

DR. MILLER: I should like to refer briefly to a case of meningococcus meningitis in almost a new-born baby (2 weeks old), whose first symptom was an attack of conjunctivitis, which was diagnosed as of gonococcal origin. I saw the child a week later. It had received at birth silver nitrate instillations. Three weeks afterward, it began with a conjunctivitis, which got well in three days. The smears made were not stained. In a week it developed fever (in the fourth week) and stiffness of the neck. Although six lumbar punctures were made, physicians were unable to come to any conclusion, because only one or two drops of gelatinous fluid appeared at the puncture. This material was sterile. The lumbar puncture fluid was procured by Dr. J. A. Kolmer of Philadelphia. Afterward I made a ventricular puncture, which revealed the meningococcus. The child died. A blood culture from the jugular vein was also made in this case. It also was sterile. I have referred to this case as being interesting because the first diagnosis was gonococcus meningitis, but this was found to be incorrect, the organism being the meningococcus.

DR. HERRMAN: The case that I reported last year was unusual, because the child did not even have one convulsion. If a baby has a convulsion, we should be justified in making a lumbar puncture for diagnostic and therapeutic purposes, but the fact that meningeal symptoms may be entirely absent renders it possible that instances of meningitis in very early life may not be so rare as the few reports in the literature would lead us to believe. In some cases the organism producing the meningitis is the colon bacillus. In these the infection may have been conveyed through contaminated bathing water.

DR. ABT: I should like to ask Dr. Koplik several questions. The first is whether he finds any difficulty in differentiating meningeal hemorrhage in the new-born from meningitis, and the second, whether he finds any difficulty in differentiating a meningitis from the cerebral abscess that we sometimes find in new-born babies. Third, I should like to ask whether he experiences difficulty in differentiating a sinus thrombosis, which is frequently found in the sepsis of new-born babies, from meningitis. Fourth, does he believe it possible to mistake a hemorrhage into the suprarenal capsules for a meningitis in the new-born, and last, whether he or his assistants ever experience any difficulty in hospital practice in performing lumbar puncture in the case of new-born babies.

DR. LA FÉTRA: I wish to emphasize what has already been said with regard to the frequency of meningitis as a part of general sepsis in early infancy, without the symptoms of meningitis. It occurs frequently, and if we had necropsy and did punctures more often, we should find more cases.

The second point that I wish to emphasize is the difficulty of telling from the spinal fluid how long the disease has been present. Illustrating this point, I had an interesting case last spring. A baby of 4 months, with meningococcus meningitis, had been discharged from the hospital entirely cured, with a normal cerebrospinal fluid. Two days after discharge the mother brought the

baby back with very marked meningeal symptoms, and lumbar puncture showed a fluid very thick with pus; so that we know that this pus had developed in the cord within two days. So far as I know, this observation is unique, but such an occurrence should be kept in mind as a possibility.

DR. KOPLIK: Answering Dr. Talbot's question, I would say that I know nothing about the minutiae of bacteriology. We leave that to the hospital bacteriologists, and go by their report, giving them credit for it.

In reply to Dr. Abt, I would say that when there is no temperature in the new-born, there is considerable difficulty in differentiating meningitis from ordinary meningeal hemorrhage, and it is hard to tell whether you have meningitis or not without a rise in temperature. As to sinus thrombosis, I suppose he means thrombosis of the lateral sinuses. Otitis is quite common as a secondary infection in new-born babies, from swallowing fluids, and getting them into the ear from the mouth; but as to sinus thrombosis in the new-born, I have not seen a case. The difficulty of lumbar puncture is not great. There are some cases in which it is difficult to get into the canal, but not in most. That is why the punctures were successful in these cases. Two were done in the Maternity Hospital, and the staff had no difficulty in doing them.

I wish to state that personally I am not ashamed to say that I hesitate to puncture unless I see a reason for it. I had a good lesson in regard to that lately. A boy was admitted to my service with a previous history of an up-and-down temperature. It was a difficult case to analyze, and the staff wanted to puncture, in order to see if the case was tuberculous. I advised waiting until the symptoms developed. The child got well without any interference. I hesitate to puncture a new-born infant, but if I feel that my delay will harm the baby and I am not certain of the diagnosis, I puncture.

THE USE OF SALT SOLUTION BY THE BOWEL (MURPHY METHOD) IN INFANTS AND CHILDREN

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The Murphy method of injecting normal saline solution by slow proctoclysis has been used for a few years past in adults suffering from many other diseases and conditions than peritonitis, and by medical practitioners as well as by the surgeon. My experience with it in the treatment of certain conditions in infants and children has led me to believe that it is of much more value to the pediatrist than most of us are aware of.

Although originally suggested by Dr. Murphy as an aid in the treatment of peritonitis, its advantages in all toxic conditions soon became manifest, since it was observed that when a patient with peritonitis was given salt solution by slow proctoclysis, not only did the peritonitis subside, but there was also a marked lessening of the toxemia. The latter effect is due to the fact that the large quantity of fluid absorbed dilutes the toxins circulating in the blood, and thus acts as a diuretic, promoting their elimination from the body.

For this reason it has been most successfully employed in the highly toxic states of typhoid fever. In early pneumonia, too, it appears to afford great relief, but in the later stages, after the heart has been affected by the toxemia, the blood pressure has become high, and there is obstruction in the lungs, it must be used with the greatest caution.

In the acute infectious diseases toxemia may be greatly influenced by the employment of the Murphy drip, and in diphtheria and scarlet fever the resulting dilution of the toxins is of the utmost value in averting nephritic complications. In uremia and suppression of urine slow proctoclysis promotes diuresis, and thus dilutes the highly toxic and irritating materials which would otherwise be harmful to the kidneys.

Generally speaking, in toxemia from any cause, whether it be an auto-intoxication, mineral poisoning, or septicemia, the judicious use of salt solution by the bowel will prove of great value in treatment.

If nephritis with edema is present, the administration of salt solution by this method is, in my opinion, unwise, although in a few such cases it has apparently been successfully employed. Further experience in such cases is necessary before its value can be considered proved.

It has recently been used with benefit in adults suffering from alcoholism with delirium, and its use before and after etherization has been suggested.

Since nephritis in children is induced by toxins in the blood, we have in slow proctoclysis not only a prophylactic, but also a curative measure as well; for by the dilution of the toxins acidosis is decreased, the activity of the kidneys is reestablished, and improvement follows.

I have been greatly impressed, although not surprised, by the excellent results following the Murphy treatment in profuse diarrhea due to intestinal infection and in the summer diarrhea of children, the symptoms being greatly relieved when the fluid lost by the bowel was replaced. Its use in dysentery is being more widely adopted each year, while in Asiatic cholera Michael found that 40 per cent. of the patients treated with saline infusions recovered, while only 22 per cent. of those not so treated showed any improvement.

A loss of body fluid from persistent vomiting or any other cause can be replaced in whole or part by normal solution, injected into the bowel, and then absorbed. We find, too, in slow proctoclysis an invaluable aid in the treatment of cyclic vomiting, pylorospasm, pyloric stenosis, and esophageal stricture, although in the two conditions last mentioned nutritive enemas must sometimes be given alternately with the injections of salt solution in order to maintain the nutrition.

My experience with the Murphy method in treating pylorospasm has been very gratifying, and in the case of an infant 25 days old with severe jaundice, persistent vomiting, and diarrhea, the stools being largely composed of mucus, which was black, the employment of the Murphy method, as a last resort, was followed by speedy recovery.

Fischer has had occasion to employ the Murphy treatment in erysipelas, and advocates its use when there is marked toxemia and high fever. It has also been used in typhus fever.

I regard the infusion of normal saline into the bowel by the drop method as a most valuable aid in the treatment of all the exhausting diseases of infancy and childhood, and believe that by its stimulating effects threatened collapse can often be averted. In feeding children and infants who can not retain nourishment given by mouth, a nutrient

enema given drop by drop is often better retained and absorbed than when given more rapidly.

Sugar solution has recently been given by proctoclysis in cases of diabetic acidosis, in an effort to promote continuous absorption, and in some instances the acidosis absolutely disappeared.

Lesné administers artificial serum by proctoclysis, giving 50 to 100 c.c. of isotonic serum, or 4 per cent. of sugar solution, and claims that absorption is afterward as rapid as when these fluids are injected subcutaneously. He also reports excellent results in children of all ages suffering from gastro-enteritis, cyclic vomiting, acute alimentary anaphylaxis, and typhoid fever. He states that, in those cases in which hexamethylenamin or epinephrin was added, the action of the drug was better by rectum than when given by mouth.

Proctoclysis in puerperal fever and in surgery is familiar to all in the profession, but experience has shown that it is even more effectual in the treatment of surgical conditions in children than in adults. Not only does it greatly relieve postoperative thirst and nausea, but after hemorrhage from the esophagus, intestines or lungs, and when operative or traumatic hemorrhage has produced only mild symptoms, the absorption of large quantities of saline solution from the bowel quickly replaces the fluid lost by hemorrhage.

There are three essential points in giving salt solution by the Murphy method: First, the solution must be under very low pressure; second, there must be a free to-and-fro movement between the reservoir and the rectum; third, the solution must be warm when introduced.

To guard against too great pressure on the fluid, the reservoir containing it should not be elevated more than 12 inches above the hips, and the tube carrying the fluid to the rectum should be compressed so that the solution will trickle into the rectum drop by drop, a half-pint escaping in this manner each hour. The hips should be slightly elevated, and a medium-sized catheter may be introduced four or five inches into the bowel, or a glass tube may be used.

To secure the ready absorption of the fluid, the solution should be at a temperature of from 98 to 100 F. when it enters the rectum; as it cools it is taken up less quickly by the bowel, and at 60 F. absorption is much retarded. Since the solution cools while passing from the reservoir to the rectum, the fluid in the reservoir should be kept at a temperature of at least 110 F., this being accomplished by surrounding the irrigation jar with hot water bags. A pint of solution is placed in

the reservoir every two hours, and, at the end of an hour, when one half of it has trickled into the bowel, the flow is checked for an hour, so that the bowel may have a rest.

When there has been great loss of fluid, it may be necessary to inject the saline much more rapidly. One must be careful, however, not to overdistend the bowel; for, although distention is the normal condition of the intestine, overdistention will expel the solution.

It is also possible to give by this method so much fluid that it will produce general edema and pulmonary congestion. Therefore, whenever slight edema of the tissues is noted, the treatment should be discontinued until this disappears, when, if necessary, the infusions may be very slowly resumed.

The preparation of the saline solution is a matter of no little importance, although it frequently receives but little consideration. The usual custom is to dissolve a teaspoonful of table salt in a pint of water, which is, at best, an extremely inaccurate method of calculating, since a teaspoonful may be from 100 to 300 grains, according to whether it is a level or heaping teaspoonful.

In addition to the dram of sodium chlorid, some authorities dissolve a dram of calcium chlorid in each pint of solution. Recently the use of ordinary tap water has been suggested in place of normal saline, since it is quite as readily absorbed, and in high fever, or whenever the rectal temperature is high, relief has been afforded by injections of tap water unheated.

The length of time proctoclysis should be continued varies with the aspects of the case. In children, especially, it depends on how they tolerate the presence of the tube within the rectum. In infants the mere fastening of the tube to the buttocks with adhesive strips will suffice; but older children must be persuaded to allow the tube to remain, for it may be so annoying that a sick child will try to pull it out.

The usual duration of this treatment is from four to six days; but if the rectum is not unduly irritated, and the indications warrant it, proctoclysis may be kept up with interruptions for ten days to two weeks.

The history of the child, 25 days old, mentioned in the text, is of unusual interest.

Feb. 7, 1916: Baby G., aged 25 days, had jaundice at the age of 1 week, which gradually became more marked. There was frequent vomiting, and the child took very little breast milk. The birth weight was 9 pounds, and the

present weight is 7 pounds 14 ounces with the diaper on. The child voids very small amounts of high-colored urine.

Feb. 11: There is nausea, vomiting, retching, and nystagmus. The jaundice intense. The weight is 7 pounds 8 ounces. The stool consists almost entirely of dark mucus. At times the head is retracted and spine arched. The child passes very small amounts of high-colored urine. It is dull and drowsy, and appears to be very ill. Salt solution by bowel (Murphy's method) was begun.

Feb. 12 to 17: The child vomits less, passes more urine, and takes more breast milk.

Feb. 18: The child looks better. It nurses well, about five minutes every two hours by day; it is also given three night feedings. It passes more urine of a normal color. The stools average three daily, are small, dark, and contain much mucus. The child's weight is 7 pounds 12 ounces. The jaundice is less marked, and more salt solution is retained.

Feb. 22. There is less jaundice, and the child is not so drowsy. There was but one stool, dark in color, containing considerable mucus.

Feb. 26: The child now nurses for ten minutes at each time.

March 13: The stools contain more fecal matter.

March 20: The jaundice is almost gone. There is but one stool daily, almost normal in color and consistence. The child's weight is 8 pounds 7½ ounces.

May 12: The child is now 4 months old and weighs 13 pounds 2 ounces. There is one stool daily, and no vomiting. It nurses fifteen minutes at a time, and appears to be normal.

Feb. 11, 1916: The urine saturating the napkins showed a trace of bile. A specimen of the feces showed macroscopically that they were semisolid, of a yellowish brown color and fetid odor. There was a small amount of mucus, but no gross detection of pus or blood was possible, and there were no parasites.

Microscopically there were no crystals and no food remnants. There were traces of mucus, but no epithelial cells. There were numerous leukocytes, and a few erythrocytes, but no ova and parasites. Chemically there was some blood distinguishable and a faint trace of bile.

DISCUSSION

DR. MCCLANAHAN: My remarks are within the title of the paper rather than the subject. For twenty years I had a large obstetrical practice before I limited my practice to children. Several times I saw apparently normal infants who, on the second or third day, developed a high temperature with anuria; usually they were the children of primiparae. I found these infants while taking the breast were getting a very small quantity of milk. This I proved on two occasions by weighing before and after nursing. In these cases of inanition fever this method of treatment is excellent, indeed, life saving. In one case in which at my first visit the temperature was 105 with almost no urine, by the use of enemas by the drop method the temperature fell to normal within twenty-four hours. In other cases, such as those with cleft palate or harelip, in which the infant cannot create the act of suction and suffers from lack of nourishment from this account, this method is of value. In these cases, however, we usually resort to gavage or the giving of the breast milk by the drop method.

DR. ABT: I have never had the success that Dr. Graham has had in keeping the rectal tube in place. The baby's rectum has a low tolerance for this treatment. Very frequently one sees considerable irritation around the

tube, particularly in cases of diarrhea and cholera infantum. These babies suffer an additional insult in such cases, and I think the condition becomes aggravated instead of improved. By this method we are simply inverting the process of nature. We are giving the baby water to drink by the rectum. I conceive this to be a laborious process on the part of the organism, requiring the expenditure of cell energy and the adaptation of unusual vital processes. In a weak baby, struggling to maintain its existence, I imagine that this method of treatment would impose an increased amount of labor in the transport of water to the various parts of the body and that this increased effort might decide against the patient in the struggle. In our present state of knowledge and with the physiologic data at hand, we should not be too ardent advocates of inverting the natural feeding process.

DR. LA FÉTRA: Regarding the technic, I would say that we found that the best method was to use an inverted vacuum bottle for keeping the solution warm.

I agree with Dr. Abt that it is better to put the water in by some other way than by rectum, if this is possible. Recently Dr. Schloss has been doing some work on acid intoxication. He found that the Murphy method of introducing the solution was good, but that to give it by mouth was better, and that when one needs to get an increase in the alkalinity of the blood, the route by the longitudinal sinus was the only one satisfactory.

DR. GRAHAM: I quite agree with Dr. Abt and Dr. La Fétra that if fluid can be introduced by the stomach, that is the preferable route; but there are quite a large number of children in whom it is impossible to introduce fluid in this manner except by a tube. The treatment, in the cases in which we have employed it, was designed purely to overcome the difficulty presented by the fact that fluid could not be introduced by mouth. We naturally chose the rectum, as the fluid could not be introduced by way of the stomach.

THE ENERGY METABOLISM OF A CRETIN*

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Studies of the glands of internal secretion have shown that the thyroid gland has a very profound effect on the energy metabolism. An overproduction of the active element of the gland increases the irritability of the nervous apparatus and raises the metabolism, while an underproduction reduces the irritability of the nervous system and lowers the metabolism. The former symptoms are shown clinically in exophthalmic goiter and the latter in myxedema and cretinism.[1]

Magnus-Levy[2] established the fact that in exophthalmic goiter the energy requirements were greatly increased, being from 50 to 70 per cent. above the normal, and that in myxedema and cretinism[3] the heat production might be as low as 45 to 50 per cent. below the normal. Du Bois[4] reported briefly the results of his researches in Professor Lusk's laboratories, in which he studied the diseases of the thyroid gland and obtained similar results to those of Magnus-Levy. Du Bois says:

> In one cretin who was 36 years old, but had the mental and physical development of a child of 8, the total energy requirement was from 18 to 25 per cent. below the normal, but was raised almost to the normal on the third day of treatment with thyroid extract.
>
> The boy, C. G., who was studied in this investigation, entered the children's ward of the Massachusetts General Hospital, Jan. 18, 1915, aged 3 years and 8 months. He was born at full term, and it was necessary to use artificial respiration for ten minutes before he breathed. His parents said he weighed 14 pounds at birth. He was breast fed entirely for one year. During the second year he was given whole milk and crackers, and after that cereals and bread were added to the diet. He was unable to feed himself, could not speak any words, and was unable to sit up alone. His parents thought that he recognized them. The physical examination showed a stupid, well-nourished, fat child, with very little musculature, lying in bed with a blank facial expression. He was phlegmatic and remained quiet most of the time, but when he cried, his voice was hoarse. The hemoglobin was 70 per cent. The skin was

*From the Nutrition Laboratory of the Carnegie Institution of Washington, and the Children's Medical Department, Massachusetts General Hospital.

1. Lusk: Science and Nutrition, Ed. 2, Philadelphia and London, 1909, p. 268.
2. Magnus-Levy: Berl. klin. Wchnschr., 1895, xxxii, 650.
3. Magnus-Levy: Ztschr. f. klin. Med., 1904, lii, 201.
4. Du Bois: Jour. Am. Med. Assn., 1914, lxiii, 827.

pale, sallow, dry, thickened, and wrinkled. The hair was coarse, bristly and dry. The anterior fontanel, though closed, still showed a depression. The tongue was thick, and protruded from the mouth most of the time. The extremities were shorter than normal; the hands square and thick, the skin over them being wrinkled. There was a slight umbilical hernia, and there were marked supraclavicular pads of fat. Otherwise the physical examination was normal, except for a systolic murmur heard over the whole precordia. He was the typical picture of a cretin, with the mental development about that of a four to six months old infant. His weight on entrance was 11,800 gm.

Fig. 1.—Metabolism of cretin, C. G.

His energy metabolism was studied after feeding, in the apparatus furnished by the Nutrition Laboratory of the Carnegie Institution of Washington.[5]

Since he was larger than the infants for which the chamber had been planned, there was very little room to spare after he was in it. This, however, did not seem to bother him during the first observations, on January 19, when two very quiet periods were obtained, and are

5. The technic has been previously described by Benedict and Talbot: Carnegie Publication 201, 1914, p. 32.

marked with a star in Table 1 as minimum periods. On January 30, after a course of ten days' treatment with thyroid extract, he had improved very markedly, showed more intelligence, became more active, and showed signs of discomfort in his restricted quarters. He was relatively very active and it was impossible, unfortunately, to get minimum periods for comparison after he was treated.

TABLE 1.—ENERGY METABOLISM OF C. G., CRETIN

Date, 1915	Body Weight and Surface	Height, Cm.	Heat Produced per 24 Hours, Calories			Average Pulse Rate	Relative Activity
			Total	Per Kilogram	Per Square Meter Lissauer		
Jan. 19	11.83 Kg.	85	460†	..	.....	94	Quiet
	$10.3\sqrt[3]{\overline{a^2}} = 0.535$ sq. m.		464	39	867*	95	Quiet
			497	42	929*	95	Very active
			616	52	1,151	116	
Jan. 30	10.78 Kg.	85	672	..	.....	119	Very active
	$10.3\sqrt[3]{\overline{a^2}} = 0.503$ sq. m.		725	67	1,441	127	Very active

* Minimum periods of heat production, pulse and activity.
† Preliminary period, not used in calculations.

TABLE 2.—COMPARISON OF METABOLISM OF THE CRETIN C. G. WITH THAT OF TWO NORMAL INFANTS

Name	Age	Body Weight Without Clothing	Height, Cm.	Heat Produced per 24 Hours, Calories		
				Total	Per Kg.	Per Sq. M. Body Surface, Lissauer
Normal Infants:						
R. L.	8½ mos.	7.58	71	455	59	1,140
E. G.	10 mos.	9.37	74	480	41	1,046
Creatin, C. G. ...	3 yrs. 8 mos.	11.83	85	479*	40.5*	898*

* Average of two quiet periods.

The lack of data of the metabolism of normal children makes comparisons of the metabolism of C. G. less satisfactory. Table 2, however, is given to show his metabolism compared to two healthy infants, one of which was aged 8½ months, and the other 10 months.

Table 2 is given for comparison because there are no available figures of normal children during the fourth year of life. It is obviously valueless to compare C. G.'s metabolism with that of the adult or with that of Du Bois' 36-year-old cretin. One might speculate as to how the metabolism of C. G. would compare with that of an infant of his own age. In place of that, Table 2 is given as the most available substitute.

The total metabolism for twenty-four hours of these three babies was not very far apart. The comparison of the metabolism per square meter of body surface and per kilogram of body weight is of greater importance since it shows that in both instances the metabolism of the cretin is at least 25 per cent. lower than that of the two infants. Since the cretin was a fat, phlegmatic individual, who did not move much, one would expect that his metabolism would be lower than that of a well-muscled, active baby.[6] It is evident that he was living on a very low plane and that his energy metabolism was considerably lower than what one would expect for a child of his age. These results, while inconclusive, because of the scarcity of material for comparison, are consistent with the findings of Du Bois and others.

DISCUSSION

DR. SEDGWICK: I had the pleasure of going through Dr. Talbot's hospital a month ago, and found him doing very good work. If you have the opportunity, you will find it very inspiring to visit that institution. Along this line, we are doing routine work on creatin-creatinin. We are doing it more or less blindly on all the subjects that we can get hold of, and have 700 unpublished records. One was a case of hypothyroidism in a child of 9 or 10 years, who was thought by people generally to be but 4 or 5. We tried giving this child desiccated thyroid, and found that the excretion of creatin-creatinin jumped up markedly. This is an indication of increased metabolism, I think, in these cases.

DR. TALBOT: I shall be very glad to show what we are doing to any one who comes to Boston before the middle of June, when the laboratory takes a vacation for the summer.

Dr. Sedgwick's observation about the increased excretion of creatin and creatinin is interesting, because there seems to be some connection between these bodies and the energy metabolism. Where that clew will lead no one knows, but it looks as if there were a connection between one of these bodies and the amount of active protoplasmic mass in the body, which also influences the amount of metabolism.

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6. Talbot: The Energy Metabolism of an Infant with Congenital Absence of the Cerebral Hemispheres, Arch. Pediat., 1915, xxxii, 452.

MULTIPLE SCLEROSIS IN A CHILD OF FOUR AND ONE-HALF YEARS

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L. W., colored, 4½ years of age, visited the outpatient department of the Children's Hospital March 2, 1916. Her chief complaint, as voiced by the mother, was nervousness. Her family and social history showed that her mother was nervous, though she gave no history of stillbirths or miscarriages, and was otherwise negative. The social service nurse reported that this was the only child of an intelligent, devoted mother. The home was very comfortable, warm and clean. There were more than the usual comforts. An elderly woman, the aunt, cared for the child when the mother was out at work during the day.

The child had a natural birth at full term, and was apparently healthy when born. The mother stated that the child had always been well, never having showed any signs of nervousness, her chief complaint at the time of entrance, excepting at the age of 2 years, when she pulled a lighted lamp from the table. This accident resulted in no harm to the child, but she was described as being irritable for some time thereafter. The tonsils and adenoids were removed one year before entrance. There was no history of a fall or injury of any kind. She had always been active and of a good disposition until the beginning of this illness, when she became droopy and wished to be left alone. There was no history of refrigeration during the winter months.

The trouble complained of came on so gradually that the mother did not notice it until her attention was called to it by friends. Apparently the illness dated back about six weeks. The so-called nervousness had grown progressively worse until at the time of entrance she was greatly troubled with shaking of the body and limbs, inability to sit still or walk and total incapacity for feeding herself.

Examined in the dispensary on her first visit, the chief symptoms presented were nystagmus, shaking of the whole body when told to stand or walk, exaggeration of all reflexes, heart rapid, but not enlarged.

Ten days later these symptoms seemed to have grown worse. It was noted that the child could not stand on the tips of the toes without falling or having a tendency to fall; the gait was very uncertain; she fell down stairs after her last visit.

One week later, on March 21, she was admitted to the house service.

Examination at that time revealed a poorly developed girl, weighing 35 pounds. There was dorsal decubitus. The mental faculties seem dulled, but she could answer simple questions involving a sentence of but two or three words, after a prolonged interval of delay subsequent to the command. Her speech was thick, her words pronounced with seeming effort and explosively, with a marked staccato quality, the so-called scanning speech (bradylalia). She initiated speech with apparent difficulty, but repeated rather better the words spoken to her by the examiner.

While lying in bed she was perfectly placid and quiescent. On attempting

to sit up, there was immediately initiated by such effort extensive, coarse muscular tremor involving the muscles of the neck, the arms, the trunk, and to a lesser extent, the legs. When she attained the sitting position her balance was maintained by propping up the body on her extended arms, and this entailed such sustained effort that the intention tremor persisted while she sat erect. There was a vertical oscillation of the head as well as lateral rotary movements.

She stood and walked only when partly supported by the nurse or steadied by grasping both of her hands. While standing erect she was tremulous, but her muscular excursions were not extensive. On being commanded to walk, which she did with a marked ataxic gait, the tremor was greatly accentuated; the legs were advanced in jerky, incoordinated efforts, but progress could be attained if assisted. She was unable to stand without some support by the nurse and if this assistance was but slight, the efforts of the child to ensure her equilibrium brought on more widespread tremor. Closure of the eyes did not seemingly increase the tremulousness.

The drinking test gave rise to a typical volitional tremor. The glass was seized firmly in the hand and brought toward the lips by a series of spasmodic efforts, while at the same time, the head was advanced to meet the oncoming glass, nodding constantly, and finally the lips were plunged into the water with a resultant bespattering of the dress front.

The tremor was entirely intentional or volitional. When placed again in bed or in a chair with the body supported, the muscular movement ceased.

There was lateral nystagmus almost constantly present and exaggerated on voluntary movement of the eyes. The pupils reacted normally and the eyegrounds were reported negative by the ophthalmologist.

The tongue showed marked tremor when protruded, but there was no deviation. There was marked elbow-jerk, and heightened epigastric reflexes. The patella-jerks were greatly exaggerated. An ankle-clonus was present in both extremities; Babinski absent. There were no paralyses. The cutaneous sensation of pain was unimpaired and skin reflexes seemed exaggerated throughout.

The heat and cold sense was apparently normal excepting over the right thigh and leg, where there was some disassociation of the senses. There was no asteriognosis. There was incontinence of urine and occasionally of feces. The heart and lungs were apparently normal; the urine normal excepting for the presence of a few white cells. The leukocytes were 5,000.

Blood Wassermann and spinal fluid Wassermann were both negative. The spinal fluid was clear under moderate pressure, there was no increase in protein content, and the cell count was 33.[1]

After her stay in the hospital the child had an attack of chicken pox and was kept in bed for a large part of the time in a room by herself, and there seems to have been an amelioration of her symptoms, especially the tremor. She can now even feed herself, although with difficulty.

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1. A subsequent examination of the spinal fluid revealed it to be clear and colorless, it flowed rapidly, and the pressure was slightly increased. About 7 c.c. were withdrawn. The Wassermann was negative, as was the colloidal gold test. Fehling's solution was reduced. There was no increase in globulin. There were 9 cells per c.mm. (Fuchs-Rosenthal). Differential blood count showed lymphocytes 40 per cent., endothelial cells 55 per cent., polymorphonuclears 5 per cent.

Multiple sclerosis, known by its other synonyms as diffuse sclerosis, insular or disseminated sclerosis, sclerose en plaques, occurs so infrequently in children that we have considered the presentation and recording of this case to be of some interest.

Sachs[2] states that "insular sclerosis does not generally come on until very nearly the first decade of life is passed."

The Index Catalogue of the Library of the Surgeon General's Office, complete to 1906, contains but thirty-one references under the heading, "Multiple Schlerosis in Children." Among this list there are but four English and American writers included, and we are convinced that the report by one of these has no place under this designation.[3]

Collins[4] claims that the American literature is remarkably barren of clinical studies of disseminated sclerosis. He also calls attention to the infrequency of the diagnoses of multiple sclerosis (referring to cases of all ages) in this country as compared to Europe and attributes this to the failure to recognize atypical cases. In his recorded list of cases there appear one at the age of 6, two at 12, one at 13 and one at 14.

Among the earlier writers Stieglitz reports three cases in children and cites from previous literature reports by Schuele in 1871, Dreschfeld, Pollard and Bristowe in England, and Hoedemaker (from Erb's clinic), as well as Marie's collection of thirteen cases in 1883. Stieglitz was able to collect thirty-five cases up to the time of his report (1898).

L. H. Mettler[5] has contributed to the literature in this country on several occasions, devoting himself to the subject as a whole and also considering critically the question of diagnosis.

Two of the most important communications of recent years are those of Rochigneaux,[6] who collected sixty-seven cases, and Gaenlinger,[7] who analyzed seventy-five cases, many of them included in the bibliography of the preceding writer.

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2. Sachs, B. T.: Treatise on the Nervous Diseases of Children, New York, William Wood & Co., 1895.

3. Barbour, P. F.: Pediatrics, 1901, xii, 54. Norbury, F. P.: Med. Herald, 1899, New Series, xviii, 520. Officer, D. McN.: Intercolonial Med. Jour., Australasia, 1903, viii, 347. Stieglitz, L.: Am. Jour. Med. Sc., 1898, New Series, cxv, 146.

4. Collins, J.: Am. Jour. Med. Sc., 1914, cxlviii, 2195.

5. Mettler, L. H.: Symptomatology of Multiple Sclerosis, Jour. Am. Med. Assn., Aug. 16, 1913, p. 474; Multiple Sclerosis, Ibid., Nov. 2, 1912, p. 1607.

6. Rochigneaux, J. M.: Thesis, Bordeaux, 1907.

7. Gaenlinger, H.: Ann. de méd. et chir. inf., 1909, xiii, 113; Echo méd. du nord, 1909, xiii, 37.

We are of the opinion that the case herewith presented falls within the category of the disseminated scleroses. It measures up by signs and symptoms with the syndrome of sclerosis. In its symptom picture it gives evidence of rather widespread involvement of the nervous structure, with resulting impairment of function, rather than a focal lesion or collection of lesions, with much actual destruction of nerve elements, for there are no paralyses.

THE DANGERS TO HOSPITAL EFFICIENCY FROM DIPHTHERIA CARRIERS

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PRELIMINARY REMARKS

DR. ADAMS: In presenting this paper I will say that many hospitals have had their efficiency crippled in this way, and this has been so in the Children's Hospital here, on several occasions. The most recent was due to diphtheria, but we have had similar trouble from scarlet fever, whooping cough, chicken-pox, etc. Our efficiency has been so crippled, in fact, as to cause the staff a great deal of annoyance. Fortunately, we have connected with the hospital a board of managers that is most liberal in its ideas, so far as the medical status of the institution is concerned. Its members do not interfere with medical affairs at all; but we are one of many institutions in which the things that are most desirable cannot be obtained on account of lack of funds. Like many other institutions in this country, we have been particularly embarrassed since the beginning of the war by the fact that contributions have been diverted from home charities, and our hospital has suffered materially on account of funds having been raised and sent out of this country to aid others, while our own sick are not getting the comforts that they should have.

We have asked for improvements several times, but each time have been told that there was no money available for the purpose; so Dr. Leech and I have conceived the idea of bringing before this Society a situation that we think is of some interest, and we shall be glad of suggestions as to how to remedy it.

For four weeks the institution has been closed on account of diphtheria carriers. We have had seven nurses, a hospital physician, the superintendent, domestics and forty children quarantined on account of a carrier alone, one case of diphtheria having got into the ward. (After these preliminary remarks, Dr. Leech read the written paper.)

In a consideration of the dangers to hospital efficiency from any source, we take it that it is well to first consider what constitutes hospital efficiency, and then take up the particular source which in our opinion has shown itself to be a menace to our general plan. Further, it will be well to consider what means should be taken to prevent further trouble of this kind.

Hospital efficiency should start with the president of the board of directors of the hospital and extend to the orderly at the hospital door. In other words, there must be team work between the highest in authority and the most humble employee.

To have satisfactory efficiency many things must be considered. The time allotted to us will be entirely too short to go into these matters except in the briefest way.

The president of the board of directors of all hospitals should be chosen with a view to his personal interest in all things connected with the institution. He should be a man who has been well trained in the handling of men and affairs.

The executive committee should be a body composed of those members of the directors who are in close touch with the interests of the institution from every point of view. A representative from the medical staff should always be present at their meetings to express the views of that body, not in an aggressive way, but with the idea of keeping harmony between all in authority.

Every hospital should have a trained medical superintendent, who should have exclusive control of all matters relating to the hospital, the welfare and general supervision of patients, the work of the hospital interns, and the outpatient department.

A superintendent of nurses, who has shown exceptional ability in her work as a teacher and director of young women, should be chosen.

The members of the medical staff should be medical men who have been promoted from dispensary work, or who, by reason of their attainments elsewhere, have shown particular aptitude for the positions to which they are appointed. A representative from the executive board should be present at their meetings for the same purpose that the medical staff is represented in the executive committee's meetings.

Hospital interns should be chosen by competitive examination, and have every opportunity to do work under the direction of the medical superintendent and the medical officers on duty.

Nurses should be chosen from applicants who have had sufficient preliminary education to assure of their ability to grasp, not only the ward work that they are required to do, but also the lectures which they are compelled to attend.

Employees should be under the control of the superintendent and amenable to discipline and control by him.

Social workers should be provided for follow-up work, not only for the hospital, but for the outpatient department.

Efficiency experts should from time to time be engaged to check up the work and criticize the same, from the president of the board of directors down to the orderly at the door.

If the foregoing suggestions were strictly carried out in all hospitals, it would be perfectly easy to look after the other details of hospital efficiency.

Hospital efficiency resolves itself into the proposition of doing everything for the comfort and cure of the patient, and keeping him well, after leaving the hospital for a specific period by the best modern means with a minimum cost, that is within keeping with the best interests of the medical staff, the proper use of the wards for teaching purposes, and the training of interns, medical students, and nurses.

With an organization such as we have outlined, we feel confident that there should be no trouble in carrying out our hospital efficiency in a satisfactory manner under ordinary conditions.

However, there are always conditions that may arise to interfere with our well-laid plans for efficiency, and to our minds one of the most serious dangers that menaces us in small hospitals is the diphtheria carrier.

At the Children's Hospital in this city we have recently had an experience of this character which has led us to bring this subject to your attention today. We are well aware of the fact that we are laying open the carrying out of our efficiency to criticism, but we can assure you that it is not a lack of the proper knowledge of what we should have, but an inadequate financial basis to carry out our ideas.

On April 9, 1916, a white girl, aged 21 months, who had a lobar pneumonia affecting the entire right lung, having had the initial chill on March 30, 1916, developed a slight dyspnea, which we were unable to explain, as the temperature had been practically normal for the two preceding days, with a general subsidence of the signs of consolidation. A culture was made from the throat, and the following morning a positive report was received. Antitoxin was given, but the patient died within a few hours. In the same ward a white boy, aged 18 months, a feeding patient, also developed a slight dyspnea, and a culture was taken the same day. This also proved positive. No clinical signs developed, but a postpharyngeal abscess was found and opened, the patient clearing up promptly. It was then decided to culture the whole house. As a result of this, fifty-one positive cultures were found out of a total of 100 made, including all employees, interns, and nurses. Schick tests were done on all positive cases, with twenty-four positive reactions. We immediately had all persons showing positive diphtheria cultures isolated in two wards. Those giving positive

Schick tests were placed together. All wards were closed for the reception of new cases.

Cultures have been taken at intervals of three days, from that time to the present, and so far we have reduced our number of positives to seventeen. Only one case has shown any clinical evidence of diphtheria, this being a white boy, aged 10 years, suffering with a broken arm. He showed a positive Schick test. The only symptom found in this case was a slight exudate on the left tonsil. He was given 3,000 units of antitoxin and within two days his throat was clear. He remained positive for the Klebs-Loeffler bacillus for twenty-four days.

Our wards were closed for the reception of new cases for a period of three weeks, and, in fact, one ward is still closed.

Now the question arises, what was the original source of the infection? In looking over the situation, we found that a nurse on duty in the baby ward had, about ten days previously, complained of sore throat. She was not off duty, but received some treatment from one of the head nurses. Her culture was positive and remained so for twenty-six days. When the cultures were made it was found that the baby ward was the greatest source of trouble. Eight positive cultures were found there, out of a total of twelve babies. Seven nurses gave positive cultures, who were distributed through the other wards. As no cases of diphtheria had been present in the hospital for many months, we are forced to the conclusion that the original nurse was the beginning of the trouble. She had not only had charge of the babies, but had mingled freely with the other nurses, and they, in turn, had been on duty in the other wards, thus being a source of infection to the other nurses, children, interns and employees.

The situation thus thrust on us immediately closed our wards for teaching purposes, for the admission of new cases, for the discharge of suitable cases (without further cultures), and the general interference with our system. Furthermore, it gives us a reputation with the public which is not at all conducive to confidence on their part in the future. From a financial standpoint the closure of the private wards has been a great loss.

Now for a consideration of the methods for the prevention of the recurrence of such outbreaks. First of all we must consider our ability from a financial standpoint to meet all the demands of hospital efficiency. We are firmly convinced that all institutions for the care of sick children should be provided with a suitable ward for the detention of all patients newly admitted. On account of the financial factor, we

are without such a ward, although plans have been prepared for some time for its erection.

We feel that all new patients should, immediately on admission, have nose and throat cultures taken; and be at once placed in a detention ward for a period of at least five days.

All ward patients who show the slightest symptoms of the minor contagions should immediately be placed in the detention ward and carefully watched for a proper period, and if definite symptoms of any of these conditions appear, these patients should be at once transferred to a contagious disease institution.

If it is impossible, for financial reasons, to provide a suitable detention building, cubicles should be provided in each ward and proper nursing technic carried out to prevent dissemination of the minor contagions. Nurses, interns, or employees showing any evidence of illness should be seen at once by a medical officer. If any evidence of throat, nose or laryngeal condition is present, such persons should at once have culture tests made and they should be kept isolated pending the report on the cultures.

Tests for the virulence of the organism found in diphtheria carriers should be made, thus relieving ourselves at once of a large number of patients whom it would be otherwise necessary to isolate. Dr. J. P. Sedgwick tells us that this is carried out in the Hospital of the University of Minnesota Medical School, in which detention wards are not provided and they have thus been saved much trouble from carrying patients indefinitely, and interference with admission of new patients.

Visitors to ward patients should be restricted to adults only, and such visitors admitted as infrequently as possible.

Following the suggestion of Dr. Alfred F. Hess, all infants should be kept isolated from children of the run-about age.

In conclusion, we are convinced that great danger to hospital efficiency does exist in the presence of diphtheria carriers in any children's hospital, especially if for financial reasons it is impossible to maintain it at the highest point.

We would urge that efficiency be maintained by every means possible, even if some of the work which is deemed of importance has to be curtailed as a result.

We believe that if there is perfect understanding between our different boards, all will work together for the common end and thus eliminate many dangers that threaten hospital efficiency from time to time.

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DISCUSSION

Dr. Graham: The question of contagious diseases gaining admission to teaching hospitals is important and serious. I agree with all that the writers of the paper have said, but I should like to emphasize particularly the desirability of keeping visitors out of the wards. We may have our detention room, and we may make cultures of the secretions of the nose and throat of these patients before they are admitted, but unless some adequate provision is made to exclude not only children, but also adults, from visiting the wards, most of our results will be very unsatisfactory. We have had so much trouble in Philadelphia in our teaching hospitals that we recently decided at Jefferson to allow the visitors to walk on a balcony that is constructed outside the children's wards, from which they can see the children through the window. If this plan is not practicable, as it would not be in hospitals not so constructed, I think that it would be better to have the child taken out of the ward to a convenient room in which it may be seen by its visitors. We thought seriously of following the plan adopted by some hospitals, that of allowing no visitors to the wards. It does not, however, seem fair, in this day and generation, to take a sick child and put it into a hospital and then absolutely prohibit its parents from seeing it.

Dr. Nicoll: I would suggest that if the doctor thinks of building a new isolation ward, he have it made large enough to cover the period of quarantine for scarlet fever and measles.

Dr. Freeman: In a hospital in New York in which we have been having no visiting we have just introduced once-a-week visits. It did not seem right to keep the parents out entirely.

Dr. Adams: At a recent meeting of the board of directors they instructed me to get estimates on cubicles and have them in the ward.

I will say in reply to the remarks of Dr. Gittings that I have been connected with the Children's Hospital since 1876, and that the medical staff has always ruled in medical matters. There is no interference with the staff, so far as the board of directors is concerned. They always say, "What does the staff think about this?" and whatever the staff thinks goes.

This is the last paper to be presented at this meeting, and I want to congratulate the Society, at my termination of service as secretary, on its work this year. Last year we had a good program and had fifty members present out of seventy. This year we have forty-nine present out of sixty-nine. One man is in Europe, one has resigned, two members are sick, and sixteen are unaccounted for. Of the forty-one papers on the program, we have heard thirty-seven in full and four by title. Two of the authors of the latter were here and were prepared to read their papers, but on account of the crowding they asked to have these read by title. I think that we have cause to congratulate ourselves on the fact that the Society's work has been so well done at this session, as well as the last, and I wish to congratulate the president on the expeditious manner in which he has conducted the business of the meeting. I move that he be given a rising vote of thanks.

SCHICK REACTION IN INFANTS

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AND
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The intradermal diphtheria toxin test, first described by Schick in 1909, is now generally accepted and is one of the most recent advances in modern scientific medicine. A number of competent and reliable observers have verified Schick's claims, so that now there is no question as to the accuracy of this test in detecting individual susceptibility and immunity to diphtheria.

The age factor in diphtheria is important. Clinical evidence shows that young infants, especially in the first six months of life, possess natural immunity, and that the susceptibility to diphtheria increases rapidly after the first year to the eighth, and then decreases. The results of the Schick test in children over 2 years of age show a striking similarity with the clinical frequency of the disease, but the statistics of patients under 2 years of age are meager in comparison and not at all uniform. For example, Schick found only 7 per cent. of positive reactions among 275 infants under 1 year of age, while Park and Zingher found 40 per cent. positive reactions among five infants under 1 year of age.

Table 1 shows the results of different observers in patients under 1 year of age, and from 1 to 2 years of age.

It will be seen from Table 1 that the variation under 1 year is from zero to 40 per cent., and from one to two years ranges from 15 to 65 per cent.

An investigation was made among ninety-five infants under 2 years of age in two infants' institutions and hospitals in Albany in order to ascertain their susceptibility to diphtheria. The tests were made by Drs. Youland and Van Winkle of the laboratory staff of the New York state department of health.

The technic pursued, briefly, was as follows: Standard diphtheria toxin was diluted so that 1 c.c. contained 1/5 minimum infective dose, and 0.1 c.c. of this dilution was used in making the tests. The procedure of Park and Zingher of heating one half of the diluted toxin

at 70 C. for three minutes was used for the purpose of control. The reactions were read daily for four days and the final interpretation of the reaction was made on the fourth day.

In practically no case did a typical pseudoreaction occur. This accords with the experience of others, that infants possess slight or no hypersensitiveness to foreign protein. Traumatic pseudoreactions developed in a small number of the infants, but only to a slight extent and in no way interfered in reading the tubes.

TABLE 1.—Result of Schick Test on Children of Different Ages

Observer	No. Cases	No. Negative	No. Positive	Per Cent. Positive
UNDER ONE YEAR				
Schiller	9	9	0	0
Schick	291	275	16	7
Griswold	..	..	..	7
Kolmer	25	22	3	12
Bundeson	60	43	17	28
Moffet and Conrad	20	14	6	30
Moody	48	32	16	33
Park and Zingher	5	3	2	40
Total	458	398	60	13
FROM ONE TO TWO YEARS				
Griswold	..	..	..	15
Bundeson	10	4	6	29
Moffett and Conrad	27	18	9	33
Schick	42	24	18	43
Kolmer	21	12	9	43
Schiller	14	7	7	50
Moody	36	16	20	55
Park and Zingher	40	14	26	65
Total	190	95	95	50

It is important to bear in mind, as first pointed out by Zingher, the occurrence of a delay in reaction to the toxin after it has been injected. In some cases the reaction did not occur until the third day, although it appeared more frequently on the second day.

Cultures from the nose and throat were taken on all cases. Virulent diphtheria bacilli were present in the nose in five infants. One of these gave a negative reaction to the toxin and was considered a carrier. Three reacted positively, showing the absence of antitoxin in the blood. All five of these bacillary cases had a sanguineous-purulent nasal discharge and should be considered cases of diphtheritic rhinitis.

It would seem, therefore, when virulent diphtheria bacilli are found in infants having no antitoxin in their tissues that a careful examination for diphtheritic rhinitis should be made, as in these five cases it was entirely overlooked clinically.

The results of our investigation are shown in Table 2:

TABLE 2.—RESULT OF SCHICK TESTS ON INFANTS UNDER TWO YEARS OF AGE

	Total	Negative	Positive	Per Cent. Positive
UNDER ONE YEAR OLD				
St. Margaret's House and Hospital for Infants	40	21	19	47.5
Frances Elliott Infant Home	26	14	12	46
Total under 1 year	66	35	31	47
FROM ONE TO TWO YEARS OLD				
St. Margaret's House and Hospital for Infants	19	8	11	57.9
Frances Elliott Infant Home	10	4	6	60
Total 1 to 2 years	29	12	17	58.6

These results are remarkably similar and agree very closely with those reported by Park and Zingher.

At St. Margaret's Hospital there are annually several cases of clinical diphtheria among the nurses, and a test of seventeen nurses gave a positive reaction in seven and four reacted negatively. Three had a typical pseudoreaction, and three had combined pseudo and positive reaction. Weaner and Rappaport have given the Schick test to all nurses entering the Durand Hospital for the last two years. Those showing a positive reaction were given 1,000 units of antitoxin and were retested every month, and reimmunized if a positive reaction again appeared. Since this procedure was adopted they claim that no case of diphtheria has occurred among the nurses.

An extremely puzzling feature at St. Margaret's was the case of an infant, R. S., 8 months of age, who reacted negatively to the Schick test and had a negative throat, but positive nose cultures. Two days later this child developed what was considered catarrhal croup, which grew worse rapidly, and 5,000 units of antitoxin were injected at 5 p. m. At 8 p. m., after tracheotomy, the child died. Examination of the larynx showed a great deal of edema, which may have been due to attempts to intubate, and a small amount of membrane. Cultures of this membrane showed Klebs-Loeffler bacilli, which were found to be

virulent to guinea-pigs. This is the only instance which we can find in the rather voluminous literature which has appeared since 1909 in which a negative Schick reaction has been followed so closely by clinical diphtheria.

In a paper read before the Albany County Medical Society in November, 1900, one of the writers described the value of antitoxin in producing immunization. At St. Margaret's, a clinical case of diphtheria occurred and cultures taken from throats of forty-eight babies showed the diphtheria bacilli in fifteen of them. All of the children were then immunized and no further cases developed.

Outbreaks of diphtheria in infants' hospitals and institutions twenty years ago were not at all infrequent, and were of very serious import. The use of antitoxin as a prophylactic measure has now removed the dread of these outbreaks. In many of the hospitals its use was employed at the time of admission, and in not a few a prophylactic injection was given to all the children from 3 to 4 weeks old.

Today we know this is unnecessary, and that the immunizing dose should be given only to those reacting to the Schick test. There is no question but that every child, nurse or attendant entering a children's hospital or institution or coming in contact with the children in any way should have cultures taken from both nose and throat and a Schick test made as a matter of precaution against the disease.

GENERAL INDEX

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